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SCIATICA

DIFFERENTIAL DIAGNOSIS AND TREATMENT

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The term "sciatica" commonly refers to a pain which extends from the sacroiliac region into the posterior or posterolateral part of the thigh and calf or lateral portion of the leg. The pain may continue as far as the heel or even into the lateral border of the foot. This pain is almost always caused by the presence of a pathological process affecting the sciatic nerve, the lumbosacral plexus or the fourth lumbar, fifth lumbar or first sacral nerve roots. Pain that extends only from the lumbosacral junction to the inferior margin of the gluteal fold or to the midportion of the posterior part of the thigh should not be classed as sciatica and may be due to pathological processes which do not affect the sciatic nerve or any of the fibers which form it.

The diagnosis of the cause of sciatica depends on evaluation of a composite examination that includes history, physical examination, urinalysis, leukocyte count, hemoglobin determination, roentgenologic examination of the lumbosacral portion of the spinal column or the pelvis or both and, in some instances, special studies, such as blood sedimentation rate determination, cerebrospinal fluid examination and myelography. Lesions causing sciatica occur in one or more of the following sites: (1) sciatic nerve, (2) lumbosacral plexus and (3) fourth lumbar, fifth lumbar or first sacral nerve roots.

Lesions of nerve roots cause more than 95 per cent of all cases of sciatica, and more than 90 per cent of these radicular lesions are protruded intervertebral disks. Lesions of the sciatic nerve and lumbosacral plexus are uncommon but may be differentiated from those of the roots by the severity and location of the abnormal physical signs produced. For sciatic nerve lesions these are weakness or paralysis of the flexors of the knee plantar flexors and extensors of the foot and ankle, loss of the achilles tendon reflex and impairment of all modalities of sensation in the posterior part of the thigh, posterior and lateral parts of the calf and lateral surface of the foot. For lesions of the lumbosacral plexus, the physical changes are weakness or paralysis of the extensors of the knee, loss of the knee jerk and impairment of all modalities of sensation in the anterior and anteromedial surface of the thigh and anteromedial surface of the leg and foot, as well as those changes mentioned above. These physical signs are more extensive than those produced by a lesion of a nerve root. The diagnosis of trauma to these structures is made from the history and from the gross inspection of the involved parts. Neoplasm must be suspected if a mass is found in the posterior portion of the thigh, but this diagnosis can be confirmed only by gross and microscopic study of the tumor tissue. Auscultation and palpation of the mass may lead to a diagnosis of aneurysm or arteriovenous fistula. Diabetes and diabetic neuritis may be initially detected by testing of the urine for sugar. Exposure to toxic substances, such as alcohol or arsenic, may be the cause of the neuritis. Dietary deficiency can produce changes in the nerve, and arteriosclerosis may involve the nutrient vessels to the plexus or nerve, but the latter diagnosis is difficult to substantiate, as is that of primary sciatic neuritis, and should be made only after other causes for the neuropathy have been excluded.

As mentioned above, lesions of nerve roots cause more than 95 per cent of all cases of sciatica, and more than 90 per cent of these nerve root lesions are the result of protrusion of an intervertebral disk. Of course, there are many other causes of lesions of these nerve roots, including neoplasm, spondylolisthesis, fracture of a vertebra, epidural abscess, osteomyelitis, syphilis and arthritis, but any of these causes produces similar symptoms and abnormal physical signs, which together make up the radicular syndrome.

What is this radicular syndrome? It consists of pain in the lower part of the back or sacroiliac region extending into the posterior or posterolateral portion of the thigh to the knee or below into the posterior or posterolateral part of the calf. This pain may even travel into the heel, ankle and lateral side of the foot. It is described as an ache or soreness with an element of "shooting" or "traveling" from the back or hip into the lower extremity. A cough or sneeze or straining at stool may temporarily increase the back pain or may produce an extension of pain into the thigh and calf. The back is sore and stiff, and these phenomena

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become severer as the day and the patient's activity progress. The patient often finds it difficult to get comfortable in bed and may turn restlessly trying to find some position which will seem to bring relief. Sitting in a chair or riding in a car may increase discomfort, and, in the former instance, the patient may sit on one buttock, attempting to relieve the pressure on the affected buttock. There may be a sensation of numbness or tingling or other unpleasantness which most commonly is felt in the lateral portion of the calf and ankle or along the lateral border of the foot with extension into the toes. When the lesion is extensive, there may be a history of weakness of the leg, producing foot-drop, actual loss of sensation on the lateral surface of the calf, ankle and foot and impaired control of the bladder or bowel or both. The latter complaints are not commonly caused by a protruded intervertebral disk.

The radicular syndrome is characterized by a number of abnormal physical signs. Rapidly bending the head forward may produce pain in the lower part of the back with or without extension into the extremity. There is stiffness of the lower part of the back and failure to obliterate the usual lumbar lordosis when the spinal column is flexed. The achilles tendon reflex may be diminished or absent on the side of the lesion (it is best tested with the patient kneeling in a chair). Selective weakness or atrophy or both may be present in the leg (the calf is often flabby), and there may be subjective or objective impairment of sensation in the lower lumbar dermatomes. The straight leg-raising test produces pain in the posterior part of the thigh or hip, and there is limitation of the extent of the motion possible in the affected extremity.

These are the symptoms and signs which make up the radicular syndrome (lower lumbar region). Since more than 90 per cent of the patients with this syndrome have a protruded intervertebral disk, the examiner thinks of this cause first in each case of sciatica. How can one safeguard against mistakes in diagnosis in those patients who have some other cause for the radicular syndrome? There are a number of such safeguards.

Most important in the patient's history is a record of a number of attacks of sciatica over many months or years with definite periods of remission between attacks. Such definite remissions practically eliminate neoplasms, vertebral fractures, epidural abscesses and osteomyelitis from the differential diagnosis. If the clinical course is progressive and if severe pain at night is present without a remission, a neoplasm is probably present in the spinal canal. A history of sudden onset of pain, severe in character and made worse by jarring the back, accompanied with chills and fever may indicate the presence of an inflammatory process, such as an epidural abscess or osteomyelitis. Much loss of weight with anorexia and a progressive course may mean that metastasis has occurred in the spinal canal. Often the onset of the radicular syndrome produced by a protruded intervertebral disk begins with a "snap" or "catch" in the lower part of the back while the patient is lifting or bending. This may be followed by a few days of soreness in the lower part of the back and stiffness, with ultimate extension of the pain into a lower extremity or with a complete remission, only to have a similar event occur weeks or months later. However, trauma can occur coincidentally with the onset of sciatica due to any cause—the examiner must not automatically conclude that the lesion is a protruded intervertebral disk.

Another safeguard in differential diagnosis of the radicular syndrome is the general appearance of the patient. Those with a protruded intervertebral disk look well, the appetite remains good and the weight is near normal. If there is a worn look about the patient, anorexia and loss of weight, the examiner must search with extra diligence for the cause of the sciatica.

Protruded intervertebral disk seldom produces severe tenderness in the back when the spinal column is percussed with the fist. The occurrence of such tenderness is more commonly a sign of vertebral involvement by neoplasm or infection.

Rectal examination may reveal the origin (carcinoma of the prostate) of a vertebral metastasis in a middle-aged or elderly man. Of course a small carcinoma may not be palpable; a normal rectal examination does not absolutely exclude such a diagnosis.

Roentgenograms of the lumbosacral portion of the spinal column must be made routinely. Narrowing of the lumbosacral joint is not often significant, but narrowing of the interspace between the fourth and fifth lumbar vertebra is additional evidence of disk protrusion. Only such films will make possible the diagnosis of certain diseases such as spondylolisthesis, vertebral fracture, brucellosis and vertebral metastasis.

Examination of the spinal fluid may be of general aid but should not be the sole method used for establishing a diagnosis. The spinal fluid protein may be of normal quantity in the presence of massive disk protrusion, while elevation of this value may be caused by tumor or epidural abscess. Therefore a normal spinal fluid protein does not exclude the diagnosis of a protruded disk, nor does an elevated spinal fluid protein indicate that the cause of sciatica must be a protruded disk. This examination is an adjunct to diagnosis, not a specific aid.

Myelography is a specialized technic which may assist the examiner in locating the lesion exactly and, in some instances, in determining the type of lesion present. The myelogram may be normal even though a protruded disk be present or may show a defect which cannot be verified at the time of operation. The accuracy of myelography varies, depending on the experience of the physician, and this procedure cannot be used as a substitute for the careful evaluation of an accurate history and physical examination. In many instances of disabling radiculitis it is a mechanical preliminary to surgical exploration used principally to locate the extent and the site of the lesion.

Diagnosis of the cause of sciatica depends then on determination of the site of the lesion. In 95 per cent of such cases one or more nerve roots will be affected and all the skill of the examiner must be used to detect accurately those nerve root lesions not produced by a protruded intervertebral disk.

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TREATMENT

The treatment of sciatica may vary greatly depending on the cause of the lesion. When the etiological agent affects the sciatic nerve and is some toxic substance, such as lead, the contact with the heavy metal must be stopped and dimercaprol U. S. P. administered to the patient. Diabetes must be brought under rigid control, and vitamin B_{12} may be given when the symptoms are associated with this metabolic disease. When a malignant process invades the sciatic nerve or lumbosacral plexus, it must, if possible, be removed, and if this cannot be done roentgen palliation may be attempted.

The treatment of lesions affecting the nerve roots may be divided into the therapy of all causes of radiculitis other than protruded disks and the treatment of the protruded disk. In the former group there is need for a specialized type of treatment—surgical treatment for tumors, special orthopedic management for spondylolisthesis, antibiotics and sulfonamides for acute osteomylelitis, immobilization for fracture and palliation for malignant involvement of vertebral bodies. In the latter group (patients with protruded disk) are 95 per cent of all patients with sciatica.

Therapy of a protruded intervertebral disk is of two types—conservative, or nonsurgical, and operative removal of the involved disk. There are a few absolute indications for advising operative removal of the protruded disk. Rarely, massive protrusion of disk substance will produce sudden, partial or complete paralysis of motor function and loss of sensation. When this does occur, immediate operation must be recommended. When there is progressive muscle paresis and gradually decreasing sensory function, operation in the near future is the treatment of choice. In other instances operation is an elective procedure, and the patient should be so advised. As in other elective procedures, the patient must be a willing part of the decision to remove the protruded disk—after adequate explanation of the situation by the physician. The elective indications for advising surgical treatment are (1) an extremely severe protracted attack of sciatica, (2) repeated attacks of sciatica with the production of considerable incapacity, (3) failure to improve during an adequate trial of conservative treatment and (4) an economic indication—that is, a situation in which the patient cannot afford to continue conservative treatment for an indefinite period.

There is hesitancy about making a strong recommendation in favor of operative treatment when (1) there is a massive functional component to the complaints, (2) it is a mild first attack, (3) there are no physical signs of radiculitis—only a history of sciatica—and (4) the patient is not having pain—that is, is in a remission. Best results are obtained when the patient has the disk removed during a time that he is having severe pain. The apparent improvement is so great that the patient gets off to a good start on a period of convalescence which may last for months. Rather than "talk the patient into an operation," it is better that recurrent attacks make evident to him the need for operation. The physician should exercise caution when outlining the results of operative therapy to a prospective candidate for surgical treatment. It is true that removal of the protruded disk generally breaks up the chain of episodes of recurrent sciatica and more frequently permits return to previous work at nearly 100 per cent efficiency than does any other treatment; however, mild pain in the lower part of the back may continue, sciatica is not always relieved (probably 85 per cent relief) and in less than 5 per cent of cases there is recurrence of the protrusion. These facts should be mentioned to the patient before operation; embarrassing explanations after operation may thus be avoided.

There is not complete agreement concerning the indications for performing of spinal fusion in conjunction with removal of the protruded intervertebral disk. The answer to this problem awaits long term follow-up study of patients so treated compared with a group of patients having only laminectomy and with a group of patients treated conservatively. The decision in favor of or against doing spinal fusion should be made by the orthopedic surgeon working with the neurosurgeon.

The essential elements of conservative treatment of the protruded intervertebral disk are rest, use of a hard bed, administration of analgesics, physical therapy in the form of heat and massage, support to the lower part of the back and instruction concerning care of the back when the patient resumes normal or near normal activity.

Rest means complete rest in bed with the exception of bathroom privileges and getting up for meals. This should be continued for two or more weeks or until the patient is relatively free from sciatica. Various forms of traction or casts have little advantage over complete rest on a hard bed; such forms of treatment simply make it relatively impossible for the patient to get out of bed. During the first few days of rest, the patient is often particularly uncomfortable and may need considerable encouragement to continue the treatment. The regular administration of analgesics (10 grains [0.60 Gm.] of acetylsalicylic acid with or without 1 grain [60 mg.] of codeine every three or four hours) generally gives the patient considerable relief. Support to the lower part of the back may give additional help and protection when the patient is permitted out of bed. The wearing of the average corset produces relatively little limitation of movement of the lower part of the back but may be a valuable psychological support. A spring back brace actually supports the spinal column but is cumbersome, and many patients ultimately discard it. The patient should be instructed in the correct technic for lifting—to lift with thighs and pelvic muscles rather than with back muscles and a flexed spinal column. He should avoid falls, sudden strains and twists of the back. Work should be resumed cautiously and gradually.

SUMMARY

The term "sciatica" refers to a pain which extends from the sacroiliac region into the posterior or posterolateral part of the thigh and calf. It is most commonly caused by a lesion involving nerve roots in the spinal canal. This produces the radicular syndrome (lumbar region). Important abnormal physical signs of the

radicular syndrome are (1) stiffness in the lower part of the back; (2) selective weakness or atrophy in the leg; (3) subjective or objective impairment of sensation in the lower lumbar dermatomes; (4) selective diminution or absence of the achilles tendon reflex and (5) painful or limited straight leg-raising test. The differential diagnosis of the cause of this syndrome must include protruded intervertebral disk, tumors in the spinal canal, osteomyelitis, metastatic malignant growth, fracture and epidural abscess; but protruded intervertebral disks cause more than 90 per cent of all lumbar radicular syndromes.

The treatment of the protruded disk is either surgical or conservative. The latter consists in rest in bed, use of a hard bed, administration of analgesics, physical therapy in the form of heat and massage, support to the lower part of the back and instructions concerning the care of the back.

ABSTRACT OF DISCUSSION

DR. C. HUNTER SHELDEN, Pasadena, Calif.: Dr. Millikan has given an excellent review of this frequently disabling disease. From a neurosurgical standpoint, the most important question to decide is which patients should not be operated on. Once this has been decided, one is well on one's way to the solution of the problem. I believe that every patient should have the benefit of conservative treatment before surgery is considered. The patient can usually decide when conservatism ceases to be beneficial and will usually consider surgical treatment when he gets to the stage at which he is not able to do the things that he enjoys doing, even though able to do the things that he has to do. I agree with Dr. Millikan that there are certain cardinal indications for surgical treatment. The first is the presence of intractable pain that is not relieved by any other means, and the second is that one is certain that one is dealing with sciatic pain or low back and sciatic pain. Low back pain alone is no indication for consideration of a neurosurgical procedure. In addition, there should be present some objective neurological findings, the most important of which are (1) the absence of the achilles reflex, indicating first sacral nerve root involvement, and (2) weakness of extension of the great toe, indicating involvement of the fifth lumbar nerve root. Involvement of both nerve roots often occurs if a disk is completely extruded—that is, if it has ruptured through the posterior longitudinal ligament. A weakness in hopping on one foot is generally associated with extruded fragments. One consideration which comes up frequently is pantopaque* (ethyliodophenylundecylate) myelography. This probably is done with too great frequency, because it is used as a diagnostic procedure rather than one of localization. It would probably be better if a myelography were never done, unless one is prepared and plans to proceed with laminectomy if this test should be positive. Many persons operated on for a ruptured intervertebral disk are not relieved of their pain. The poor selection of candidates or too early operation accounts for many poor results. In addition, the failure of the surgeon to find and remove all the loose fragments must be considered. The disk fragments may occupy many locations. They may be in the foramen; they may migrate up and down the spinal canal, or they may even rupture through the dura.

1. (*a*) Quick, A. J.: Studies on the Enigma of Hemostatic Dysfunction of Hemophilia, Am. J. M. Sc. **214**: 272 (Sept.) 1947; (*b*) The Present Status of Platelets in Blood Coagulation, in Conference on Blood Clotting and Allied Problems, Transactions of the Second Conference, Jan. 24-25, 1948, New York, Josiah Macy, Jr. Foundation, 1949, p. 201; (*c*) The Coagulation Mechanism, with Special Reference to Interpretation of Prothrombin Time and Consideration of Prothrombin Consumption Time, Am. J. Clin. Path. **19**: 1016 (Nov.) 1949.

2. The complex includes classic prothrombin, labile factor and organically bound calcium.

3. Stewart, G. N., and Zucker, T. F.: Comparison of Action of Plasma and Serum on Certain Objects Used in Biological Tests for Epinephrin, J. Exper. Med. **7**: 152, 1913.

MANAGEMENT OF HEMOPHILIA IN GENERAL PRACTICE

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The tacit acceptance that hemophilia is a rare and mysterious disease that should be managed and treated only by specialists has no doubt been responsible for the tendency of many physicians to assume with reluctance the responsibility of taking care of hemophiliac patients. This attitude is further fostered by the unsatisfactory presentation of this disease, especially in regard to diagnosis and treatment, in the standard textbooks and treatises on medicine. As a consequence, many cases of hemophilia remain undiagnosed; the patients often receive inadequate care and become crippled as the result of hemorrhages which might be prevented or controlled.

Hemophilia is not an uncommon disease. I have studied over 20 hemophiliacs who reside in Milwaukee, and I feel certain that there are many more in this community that have not come to my attention. It is probable that the incidence in the white population is not markedly different in various sections of the country. It is to be remembered that a considerable number of hemophiliacs have the disease in such a mild form that they rarely require medical treatment and that even those who have moderately severe hemophilia may be free of hemorrhagic episodes for relatively long periods, often for over a year or more.

NATURE OF THE DISEASE

A brief outline of the new concept of hemostasis which has evolved from a series of recent studies [1] will help one to understand the basic defect of the blood that is respnsible for the hemophiliac state. Thromboplastin, which is essential for the conversion of prothrombin to thrombin, is present in the plasma as a precursor, thromboplastinogen. This agent is converted to free thromboplastin by an activator, which is derived from disintegrating platelets. The three basic reactions are the following:

1. Thromboplastinogen + platelet $\xrightarrow{\text{activator}}$ thromboplastin
2. Thromboplastin + prothrombin $\xrightarrow{\text{complex}}$ [2] thrombin
3. Fibrinogen + thrombin $\longrightarrow$ fibrin

The thrombin, in addition to converting fibrinogen to fibrin, causes labilization of platelets. As a result of this, more thromboplastinogen becomes activated and a chain reaction is initiated. Furthermore, lysis of platelets causes liberation of a powerful vasoconstrictor, which Stewart and Zucker [3] recognized even as early as 1913 as a basic hemostatic factor. In hemophilia a congenital and hereditary deficiency of thromboplastinogen occurs. As a consequence, very little thrombin is formed and relatively few platelets disintegrate. The chain reaction, therefore, fails to be initiated, and inadequate amounts of the vasoconstrictor agent are liberated.

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It is obvious that a method for the quantitative estimation of thromboplastinogen should be a valuable asset in the clinical approach to hemophilia. With the development of the prothrombin consumption test,[1a] a simple means has become available for this purpose. In this procedure, blood is allowed to clot under controlled conditions and the prothrombin remaining in the serum is determined by a modified one stage method. The amount of unconsumed prothrombin measures the degree of thromboplastinogen deficiency. The details have been recently described.[1c]

DIAGNOSIS

The diagnosis of hemophilia is made on the correlation of the clinical history, the physical findings, the family history and the results of laboratory studies. Although the diagnosis is generally easy when the condition is severe, difficulty is apt to be encountered when the bleeding tendency is not pronounced and the family history is negative for hemophilia.

engages in relatively strenuous games. Hemarthrosis generally denotes moderately severe hemophilia.

In a surprisingly large number of hemophiliacs, no positive family history is obtainable. The most notable example of this is Queen Victoria, who was a carrier but whose family history appears entirely negative. It should be remembered that the defect can pass silently through several generations of women. Furthermore, a male may have the disease in such a mild state that it may be considered subclinical, and yet he will transmit the defect to his daughters; the severity of the disease in their offspring is unpredictable. It is always hazardous to make a diagnosis of sporadic hemophilia, and it is erroneous to assume that the hereditary pattern of descendants of a person with sporadic hemophilia will be different from that of the descendants of a true hemophiliac. Fonio,[4] who has extensively studied Swiss hemophiliac families, has likewise concluded that many apparently sporadic cases are hereditary and transmitted by persons with a latent form of the disease.

TABLE 1.—*Summary of Findings in 20 Hemophiliacs Recently Studied*

Patient	Age, Yr.	Coagulation Time (Lee White), Min.	Prothrombin Consumption (Quick), Sec.	First Hemorrhage: Age	First Hemorrhage: Occasion	First Hemorrhage: Hemarthrosis	First Hemorrhage: Epistaxis	Transfusion	Hereditary History
H. J.	22	22	12½	6 mo.	Myringotomy	+	Infrequent	+	+
J. K.	2	15	8	.....	Circumcision	0	0	+	—
D. K.	2	25	12	.....	Circumcision	+	0	+	—
K. F.	6	15	14	2 yr.	Incision of furuncle	0	One attack	0	+
W. G.	35	40	8	1½ yr.	Head injury	+	Infrequent	+	+
C. W.	1½	25	10	1 yr.	Deep hematoma	0	0	+	+
R. M.	3	10	13	.....	Circumcision	+	0	+	+
J. B.	2	40	9	.....	Circumcision	0	0	0	—
J. H.	8	15	12	.....	Oozing from umbilicus	+	0	+	—
T. B.	3	11	9	.....	Circumcision	0	0	0	—
W. C.	6	65	9	6 mo.	Multiple bruises	+	0	+	—
G. S.	4	80	9½	.....	Circumcision	0	0	+	—
R. A.	1	45	10	.....	Circumcision	0	One attack	0	—
R. K.	39	22	10	7 mo.	Bruising	+	Occasional	+	+
T. D.	8	8	11½	1 yr.	Cut lip	0	0	+	+
L. H.	26	38	9½	1 yr.	Bleeding from mouth	+	Frequent	+	+
W. S.	31	60	8	3 yr.	Injury of mouth and teeth	+	Occasional	+	+
N. S.	33	30	9	3 yr.	Cut on foot	+	0	+	+
L. K.	13	90	8	6 mo.	Hematoma from blow	+	Occasional	+	+
R. B.	11½	22	12	.....	Circumcision	0	0	0	—

Since the disease is congenital, the bleeding tendency is present at birth, even though it may be latent. Many of the patients have their first excessive bleeding after circumcision, as seen in table 1. Easy bruising after minor blows and bumps is a common observation in this disease. Characteristically, the discoloration of the skin often appears only after several days following the blow, since the bleeding is often deep, whereas in true purpura the formation of ecchymoses is prompt. It is not uncommon for hemophiliac boys to have numerous black and blue spots. These must not be mistaken for purpura. In one instance, hemophilia was diagnosed as thrombocytopenic purpura on a dubious thrombocyte (platelet) count and splenectomy was advised, which fortunately was not carried out. Frequently hematomas are formed, and occasionally the hemorrhage may spread widely by dissecting its way through soft or yielding tissue. Epistaxis, contrary to the generally accepted belief, is not particularly frequent, as can be seen in table 1, in which 20 typical cases of hemophilia are summarized. Abnormal bleeding after a tooth extraction or a minor operation sometimes is the first manifestation and, in some cases, the only sign of a bleeding tendency. Bleeding into joints usually first occurs after the boy begins walking and

The laboratory offers valuable aid in the diagnosis of hemophilia. The coagulation time is usually prolonged, provided the test is done on venous blood carefully collected to avoid contamination with tissue juice. The clotting time methods based on capillary blood are worthless and misleading. Robbins [5] recently reported on a sailor in the United States Navy who, after several hospitalizations for abnormal bleeding, reenlisted and was found physically qualified for duty. The diagnosis of hemophilia was not made because the coagulation time of capillary blood was always reported normal.

The prothrombin consumption test [6] is far more specific than the coagulation time for hemophilia and, furthermore, is quantitative. One must emphasize,

4. Fonio, A., and Passet, R.: Die sporadische Hämophilie in der Schweiz, Arch. d. Julius Klaus-Stiftg. f. Vererbungsforschg. **23**: 425, 1948.

5. Robbins, J. J.: Hemophilia: Report of a Case, U. S. Nav. M. Bull. **49**: 1115 (Nov.-Dec.) 1949.

6. In the prothrombin consumption test, 2 cc. of freshly drawn blood is transferred to each of three test tubes. The blood is allowed to clot, and after standardized time intervals the tubes are centrifuged for separation of the serum from the clot. The prothrombin remaining in the serum is determined by a modified one stage procedure.[1c] The greater the quantity of available thromboplastin in the blood, the more prothrombin will be consumed and the longer will be the prothrombin time of the serum. In hemophiliac blood very little thromboplastinogen is present; therefore, little prothrombin is converted to thrombin.

however, that it is a sensitive test, and unless the directions are followed exactly as outlined misleading results are apt to be obtained. In table 2, the prothrombin consumption of three hemophiliacs is given. The first, with a uniform prothrombin consumption time of eight seconds, presents the severest type of hemophilia, whereas the third is an example of the patient with a very mild type, who has a family history positive for hemophilia but has only minor bleeding episodes.

The prothrombin consumption test has been particularly valuable in the diagnosis of hemophilia in newborn babies. It is exceedingly difficult to collect blood from a small infant without some admixture of tissue juice and, therefore, a normal clotting time is obtained, even though the child may be severely hemophiliac. The cases to be reported illustrate the fact that the hemophiliac defect is present at birth and that early diagnosis can be made.

Case 1.—J. B., born May 4, 1949, was circumcised May 7. Bleeding occurred after the operation and continued until May 11, when a transfusion of 90 cc. of blood was given. Bleeding recurred May 15 but was controlled by absorbable gelatin sponge (gelfoam*) and suture. The prothrombin consumption time on May 17 was 11 seconds; on July 6, 9½ seconds, and on November 28, 9½ seconds. On the last examination the coagulation time (Lee White) was 50 minutes. Prior to this the coagulation time was normal, probably owing to the difficulty of obtaining the blood. In December, a large hematoma developed on the baby's arm after a minor blow. The family history was entirely negative.

Table 2.—*The Prothrombin Consumption Test in Hemophilia*

	Coagulation Time, Minutes (Lee White)	Prothrombin Consumption Time,* Seconds				
			Time After Formation of Solid Clot, Minutes			
		Tube	15	30	45	60
Normal †	8	1	9	18	24	25
		2	..	16	22	23
		3	..	..	..	23
Hemophiliac 1	40	1	8	8¼	8	8
		2	..	8¼	8	8
		3	..	..	..	8
Hemophiliac 2	55	1	9	8	9½	9
		2	..	9	9	9
		3	..	..	..	9
Hemophiliac 3	15	1	6	15	13	13
		2	..	9	14	14
		3	..	..	..	11

* According to the procedure of Quick.[1c]
† Mother of patient 3.

Case 2.—B. B. was born Dec. 14, 1949. The prothrombin consumption time (December 16) was 11 seconds. Abnormal bleeding was encountered after the breaking of the adhesions of the foreskin to the glans penis. When the baby was 4 months old, a prothrombin consumption time of nine seconds and a coagulation time of 45 minutes were obtained. An older brother, 3 years old, is a typical hemophiliac with a history of several bleeding episodes (patient J. B. in table 1).

Case 3.—M. P. was born Sept. 27, 1948. Since the baby's grandfather was a hemophiliac and two of his maternal cousins are hemophiliacs, studies were made the day after birth and periodically thereafter, with the following results: The prothrombin consumption time on Sept. 28, 1948 was 50 seconds; on Oct. 27, 1948, 38 seconds, and on April 7, 1949, 32 seconds. At no time did the child show any hemorrhagic tendency, and even after a severe fall he had no abnormal bruising.

For two of these infants the diagnosis of hemophilia was made within two weeks after birth by the prothrombin consumption test and verified by the subsequent course. The second case probably is the first on record in which the diagnosis was made before bleeding occurred. The third baby, born of a mother who is a carrier, had a normal prothrombin consumption time at birth, and it has remained normal. No hemorrhagic tendency has been noted during the first 17 months of life, and it appears likely that the child will remain normal. In none of these cases was the coagulation time dependable.

The prothrombin consumption test is a valuable new means for establishing a diagnosis of hemophilia. Since the result of the test is also low in thrombocytopenia, a thrombocyte count may be necessary, particularly if the prothrombin consumption test is the sole basis for the diagnosis. If good clot retraction occurs, one can assume that the thrombocyte count is normal. Congenital hypoprothrombinemia can simulate hemophilia clinically. Therefore, a prothrombin time determination should always be made; in cases of uncomplicated hemophilia, it is normal. It should be remembered that acquired hypoprothrombinemia may occur in a hemophiliac. Likewise a thrombocytopenic purpura may be superimposed on the hemophilic condition.

TREATMENT

Nearly all the bleeding in hemophilia comes from minute arterial vessels. Small cuts that involve only capillaries rarely bleed abnormally. Capillaries, when injured, are closed by a primary contracting force and by the natural adhesive properties of injured endothelium, which is not impaired in this disease. It is likely that the latter two hemostatic factors play an important role in the control of arteriolar bleeding in hemophilia. The back pressure resulting from bleeding into tissues tends to compress the bleeding vessel, thus pressing together its wall. Adhesion may then effect a permanent closure.

This concept forms the basis for the immediate treatment following injury. The three cardinal means are cold, pressure and rest. The application of an ice bag often accomplishes singly as much as or more than a combination of other therapeutic measures. Cold causes a contraction of the blood vessels in the injured area, and this may often be effective enough to bring about permanent closure of the traumatized vessel. Pressure is also exceedingly valuable if the site of injury permits its application. The pressure bandage combined with the application of an ice bag is the most effective way to treat hemarthrosis. In addition, complete immobilization of the joint is necessary. The deep hematomas, which are of frequent occurrence in some hemophiliacs, can often be aborted by cold and pressure.

It is of utmost importance to avoid the application of heat to a newly traumatized area. By dilation of the vessels, a hemorrhage that would remain minor is made massive. Many hemophiliacs learn by experience that heat accentuates, whereas cold minimizes, bleeding. Occasionally, however, a deep hemorrhage simulates an inflammatory process and is treated as such mistakenly with hot applications. It is well, therefore, when one encounters any condition in a hemophiliac, that one determine whether it could be due to hemorrhage before making any other diagnosis.

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Fibrin foam or absorbable gelatin foam saturated with thrombin or epinephrine is useful for the control of bleeding in certain locations, such as a tooth socket. Infection complicates the management of bleeding; therefore, the antibiotics play an important role in its control.

Clinical experience should enable one to decide when to rely solely on local measures and when to treat the bleeding systemically by means of transfusion. The rationale of transfusion is as follows: Hemophiliac blood lacks thromboplastinogen, which normal plasma contains in moderate abundance. Since the agent is present only in plasma, one volume of the latter is equivalent to two volumes of whole blood. Plasma has the additional advantage that it can be given in much greater quantities than blood. Since the primary purpose of the transfusion is to increase the thromboplastinogen level of the blood, it is essential to give a relatively large amount of blood or plasma at one time. The effect should be evaluated by the prothrombin consumption test. In table 3 the effect of mixing of hemophiliac blood with varying amounts of normal blood is presented. It should be emphasized that the coagulation time as a measure for evaluation of the therapeutic effect of transfusion is worthless and can be misleading. Considerably more study is needed before the prothrombin consumption test can be critically evaluated, but it offers the first means for determination of the basic defect of hemophilia quantitatively.

Recently it has been found that the thromboplastinogen concentration of normal persons varies considerably. Although this study is still in a preliminary state, it suggests the advisability of determining of the donor's thromboplastinogen level. Thromboplastinogen is preserved in lyophilized plasma, which makes this type of plasma particularly valuable for emergencies.

Contrary to popular belief, the most important danger in hemophilia is not exsanguination but the various sequelae from the pressure of hematomas and from the bleeding into joints. Any bleeding in the throat or floor of the mouth is particularly serious, because it readily leads to blockage of the air passage and sometimes necessitates a tracheotomy.[7] Large deep hematomas often cause atrophy of muscles, nerves and even bones. If there is evidence that this is occurring, aspiration or drainage to relieve pressure is indicated. Before a surgical procedure is done, at least 500 cc. of fresh or lyophilized plasma should be given to an adult patient and proportionately small amounts to children. The effect of the transfusion should be checked by the prothrombin consumption test. If the maximum value obtained is less than 11 seconds, more plasma is indicated.

It is well recognized that the severity of the hemorrhagic tendency in hemophilia varies and sometimes even appears cyclic. This exacerbation of the bleeding state is generally not accompanied with an increase in the coagulation time or any other demonstrable alteration in the coagulation reactions. It seems, therefore, logical to assume that a change in the vascular physiology is probably responsible for the fluctuations in the hemorrhagic tendency. The administration of high doses of ascorbic acid (vitamin C) (200 to 300 units a day) and rutin (100 to 150 mg. daily) to effect a curative action on the vascular system may be suggested in lieu of any other known approach. Too little work has been done, however, on this problem to permit critical evaluation of these drugs. The use of oxalic acid in the treatment of hemophilia appears to have no rational basis. Calcium salts are worthless in hemophilia as well as in all other hemorrhagic diseases. Since hemophiliac bleeding is often deep and produces pressure on nerve trunks, excruciating pain is not unusual. The common sedative and analgesic drugs, such as the barbiturates, the salicylates, meperidine (demerol®) hydrochloride, codeine and even morphine, can be employed with the same degree of safety as in nonhemophilic patients. Because in an occasional patient slight hypoprothrombinemia develops from use of salicylates, one is not justified in withholding these valuable analgesic drugs from a hemophiliac, who often suffers from arthritic pain resulting from hemarthrosis. A patient who is on a normal diet, including greens for a source of vitamin K, can take salicylates with impunity in regard to bleeding, provided he does not have a sensitivity to the drug.

TABLE 3.—*The Effect of Normal Blood Mixed with Hemophiliac Blood on the Prothrombin Consumption*

		Prothrombin Consumption Time, Seconds			
		Time After Formation of Solid Clot, Minutes			
	Tube	15	30	45	60
Normal A	1	8	24	28	30
	2	..	10	25	27
	3	..	..	..	15
Hemophiliac B	1	8	8	8½	8½
	2	..	8	8	8
	3	..	..	..	8
Hemophiliac C	1	8	8½	8	8½
	2	..	8	8½	8
	3	..	..	..	8
Hemophiliac B, 1.8 cc. blood	1	13	14	14½	14½
Normal A, 0.2 cc. blood	2	..	12½	12½	12
	3	..	..	..	12
Hemophiliac B, 1.0 cc. blood	1	14	17	17	17
Normal A, 1.0 cc. blood	2	..	20	20	20
	3	..	..	..	14
Hemophiliac C, 1.8 cc. blood	1	12	13	13	13½
Normal A, 0.2 cc. blood	2	..	16	15	16
	3	..	..	..	14
Hemophiliac C, 1.0 cc. blood	1	18	20	19	19
Normal A, 1.0 cc. blood	2	..	22	22	21
	3	..	..	..	19

Many hemophiliacs are crippled because joints were neglected after hemarthrosis or because contractions occurred after hemorrhage into a muscle. Diathermy after hemorrhage has subsided, passive exercise and later active exercise, such as swimming, are important measures for conserving joints. All efforts should be made to prevent a joint from becoming ankylosed in an undesirable angle. Much of this problem is in the domain of the orthopedic surgeon, but if the parents of a hemophiliac child are properly educated and have the service of a family physician who handles the emergencies, the hemophiliac need not become a cripple.

SUMMARY

The number of hemophiliacs in any community is sufficiently high to warrant all physicians in general practice to be familiar with its diagnosis and treatment.

7. Any incipient hemorrhage that is apt to injure a vital structure should be treated promptly with a transfusion of fresh plasma (500 cc. for an adult).

The diagnosis is relatively easy for a subject who has a bleeding tendency, a prolonged coagulation time and a positive family history, but, by means of the prothrombin consumption test, the diagnosis can be made even in an atypical case and at birth or before any abnormal bleeding has occurred.

The application of cold and pressure to check and control hemophiliac bleeding locally is of primary importance. When local measures fail to stop hemorrhage, a transfusion of lyophilized or fresh plasma or whole blood should be given to raise the thromboplastinogen level sufficiently to provide the hemophiliac blood with some hemostatic efficiency. The prevention of contractures and crippling ankylosis of joints constitutes one of the most important problems of this disease.

ORAL USE OF CORTISONE ACETATE

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and

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The necessity for intramuscular injections has made patients treated with cortisone acetate dependent on physicians or others for their medication and has served as a disadvantage to the use of the hormone. Its clinical application would be easier and less expensive if cortisone acetate could be employed effectively by mouth, as can certain other steroid compounds (including several estrogenic substances, ethisterone [anhydrohydroxyprogesterone] and methyltestosterone).

Early experimental work indicated that cortisone extracted from adrenal cortical tissue was physiologically active when fed to small laboratory animals.[1] This suggested that cortisone acetate might be effective, to some degree, when administered by mouth to human subjects. Because steroid hormones absorbed from the alimentary canal may be partially inactivated by the liver, it was anticipated that for comparable therapeutic response the oral dose would probably be much larger than the requirements by intramuscular injection. This assumption, together with the extreme scarcity of the compound, prevented its earlier trial by mouth in patients. Recently it was announced by Freyberg and associates [2] and confirmed by Hench and his colleagues [3] that cortisone given by mouth produced striking antirheumatic response in patients with rheumatoid arthritis and that the amounts needed were surprisingly similar to the intramuscular dosage.

1. Heilman, F. R., and Kendall, E. C.: The Influence of 11-Dehydro-17-Hydroxycorticosterone (Compound E) on the Growth of a Malignant Tumor in the Mouse, Endocrinology **34**: 416-420 (June) 1944.

2. Freyberg, R. H.; Patterson, M.; Adams, C. H.; Durivage, J., and Traeger, C. H.: Practical Considerations of the Use of Cortisone and ACTH for Rheumatoid Arthritis, read before the American Rheumatism Association, San Francisco, June 23, 1950, to be published.

3. Hench, P. S., in discussion on Freyberg and others.[2]

4. Tablets of cortisone acetate, each containing 25 mg., were supplied by Merck & Co., Inc. (Dr. J. M. Carlisle, medical director).

5. The liquid suspension was prepared by mixing the saline suspension of cortisone acetate (cortone,® Merck), as supplied for intramuscular use, with a vehicle (raspberry syrup); each 4 cc. of the mixture contained 25 mg. of cortisone acetate.

6. Boland, E. W., and Headley, N. E.: Management of Rheumatoid Arthritis with Smaller (Maintenance) Doses of Cortisone Acetate, J. A. M. A. **144**: 365-372 (Sept. 30) 1950.

PRESENT INVESTIGATION

Twenty-three patients with chronic rheumatoid arthritis were given cortisone acetate by mouth in order to determine its effectiveness as compared to that by intramuscular administration. The patients were studied in two groups as follows:

GROUP 1.—This group consisted of 14 patients who had previously received cortisone acetate by intramuscular injection for long periods. Their rheumatic manifestations had been controlled satisfactorily for periods ranging from 135 to 202 days, and the maintenance doses by intramuscular administration were known and stabilized. Without interruption of therapy the patients in this group were transferred to orally given cortisone in tablet form [4]; thus direct comparisons of the doses required for the same antirheumatic effect could be made. Thirteen of the 14 patients have now received cortisone orally for periods of three months or longer.

GROUP 2.—This group was comprised of nine patients who had not been treated previously with cortisone. Four of these were given the oral medication in tablet form, and five received a liquid suspension.[5] The dosage schedule to which patients of this group adhered was the same as that recently reported by us for intramuscular administration.[6] It consisted of three stages: (*a*) a period of initial large suppressive doses (300 or 200 mg. on the first day and 100 mg. daily thereafter until the disease manifestations were adequately controlled); (*b*) a period of gradual dose reduction, and (*c*) a period of smaller maintenance dose administration. The therapeutic response was compared to that noted in other patients with rheumatoid arthritis of similar severity who had been given cortisone by the intramuscular route. Oral administration has been continued (to this writing) for more than three months in four of the nine patients and for more than two months in five.

RESULTS

Results in General.—Cortisone acetate administered by mouth was highly effective in suppressing the activity of rheumatoid arthritis and/or in holding the disease under control in 22 of the 23 patients studied.

In one patient of group 1 (C. B., table 1) with severe rheumatoid arthritis involving multiple peripheral joints, cortisone was not effective orally. Remarkable improvement (75 to 90 per cent relief) and reduction of the erythrocyte sedimentation rate from 96 to 30 mm. in one hour had been obtained from cortisone acetate given intramuscularly. With maintenance doses of 75 mg. a day, this degree of improvement had been maintained for 194 days. Three days after transfer of the patient to orally given cortisone in doses of 100 mg. per day, relapse began. The decline proceeded despite dosage increases to as high as 300 mg. a day, and the pattern of relapse was much the same as that observed in other patients after abrupt withdrawal of the drug. At the end of 12 days of treatment orally with cortisone, all the improvement gained by parenteral use of the drug was lost. The patient became febrile, was barely able to get out of bed and was unable to shave or to comb his hair; and the erythrocyte sedimentation rate rose to 92 mm. in one hour. Subsequent resumption of cortisone therapy by intramuscular injection, at first in large suppressive doses and later in amounts of 75 mg. per day, again brought and kept the rheumatic manifestations under control. We have assumed that in this single case the hormone was not absorbed sufficiently, if at all, by the intestinal tract.

Results from Large Suppressive Doses.—When initial large suppressive doses of cortisone acetate are given intramuscularly to patients with rheumatoid arthritis

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subjective improvement, with reduction of muscular and articular aching and stiffness, lessening of joint tenderness and pain on motion, increased functional capacity and a sense of well-being, is usually noted within the first four days.[7] Occasionally the response may be noted within 24 to 36 hours, but more frequently it occurs 48 to 72 hours after the first injection. Thereafter improvement proceeds day by day with further lessening of symptoms and with gradual reduction of such objective manifestations as joint swellings. Improvements in erythrocyte sedimentation rates often lag a week or more behind the clinical response. To bring the disease under satisfactory control, large suppressive doses must be continued for a number of days —the number varying roughly with the severity of the rheumatoid arthritis.[6]

the same as that noted with parenteral injection. The liquid suspension given by mouth and the tablets were equally effective, although with the former we found it more difficult to measure the dosage accurately.

Results from Maintenance Doses. — Because the effects of cortisone in rheumatoid arthritis are temporary and not curative, it is necessary (in most instances at least) to continue the administration of the hormone if improvement is to be sustained. When large doses, such as 100 mg. daily, are given for prolonged periods, the incidence of adverse hormonal side effects is high,[8] whereas when smaller daily doses are employed the number of undesirable reactions is materially reduced. To minimize adverse reactions it is more prudent to maintain satisfactory degrees of improvement with smaller doses of the hormone than to strive for absolute

TABLE 1.—*Comparison of Maintenance Dosages Required in Group 1 Patients by Intramuscular and Oral Routes of Administration*

				Intramuscular Administration			Oral Administration	
Patient	Sex	Duration of Disease (Mo.)	Severity of Disease	Average Daily Maintenance Dose (Mg.) *	Degree of Improvement †	Length of Administration (Days)	Average Daily Maintenance Dose for Same Degree of Improvement (Mg.)	Length of Administration (Days)
L. E.	F	22	Mod.	21.5	Very marked	154	25.0	100
N. D.	F	43	Mod. sev.	37.5	Marked	146	50.0	96
M. E.	F	13	Mod. sev.	42.9	Very marked	175	62.5	96
J. D.	M	81	Mod. sev.	53.6	Marked	142	62.5	99
G. R.	M	47	Mod.	62.5	Very marked	153	87.5	95
W. H.	F	28	Sev.	53.6	Marked	142	75.0	91
M. O.	F	22	Mod. sev.	62.5	Marked	202	75.0	92
L. B.	M	41	Sev.	75.0	Marked	201	100.0	98
C. B.	M	47	Sev.	75.0	Marked	194	....	.. ‡
E. C.	M	95	Sev.	75.0	Marked	168	75.0	91
P. K.	M	61	Sev.	62.5	Very marked	154	87.5	93
J. S.	F	72	Mild	32.0	Very marked	170	37.5	91
M. S.	F	132	Mod. sev.	50.0	Marked	135	75.0	91
O. F.	F	144	Mod. sev.	65.0	Marked	150	100.0	91

* Patient L. E. received 50 mg. of cortisone acetate three times a week; N. D., 75 mg. every second day; M. E., 100 mg. three times a week; J. D. and W. H., 125 mg. three times a week; G. R., M. O. and P. K., 125 mg. every second day; L. B., 150 mg. every second day; J. S., 75 mg. three times a week; M. S., 100 mg. every second day, and O. F., 130 mg. every second day. Patients C. B. and E. C. received 75 mg. once a day.

† Improvement was graded as: very marked, 90 to 100 per cent improvement; marked, 75 to 90 per cent; moderate, 50 to 75 per cent; slight, less than 50 per cent, and unimproved.

‡ Relapse began after third day on oral cortisone and continued despite daily doses of 300 mg. for several days (see text).

In the nine patients who had not been treated previously with cortisone and who received initial large suppressive doses of oral preparations (group 2), the pattern of improvement was identical to that noted from intramuscular administration of the drug in other patients, with one notable exception: in general the onset of antirheumatic response occurred sooner with oral than with parenteral administration. In seven patients 200 mg. were given on the first day in divided doses of 50 mg. each and symptomatic relief began in 6, 7, 10, 12, 24, 24 and 48 hours, respectively (table 2). Two patients received 200 mg. in a single dose on the first day, and the subjective response was noted by them in five and in eight hours. These observations suggest that cortisone may be absorbed more rapidly by the intestinal tract than it is when the suspension of crystals is injected intramuscularly. Subsequent to the initial response the rate of improvement from oral administration of the drug was approximately

antirheumatic control with large and less safe doses. Recently our results with smaller maintenance doses of cortisone acetate given intramuscularly were reported.[6] It was found that once the disease was suppressed by large doses, the subsequent use of smaller maintenance doses ranging from 32 to 65 mg. a day was sufficient to maintain some cases of severe and most cases of moderately severe, moderate, and mild rheumatoid

7. Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: Effect of a Hormone of the Adrenal Cortex (17-Hydroxy-11-Dehydrocorticosterone: Compound E) and of Pituitary Adrenocorticotropic Hormone on Rheumatoid Arthritis: Preliminary Report, Proc. Staff Meet., Mayo Clin. **24**: 181-197 (April 13) 1949. Boland, E. W., and Headley, N. E.: Effects of Cortisone Acetate on Rheumatoid Arthritis, J. A. M. A. **141**: 301-308 (Oct. 1) 1949. Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: Effects of Cortisone Acetate and Pituitary ACTH on Rheumatoid Arthritis, Rheumatic Fever and Certain Other Conditions: A Study in Clinical Physiology, Arch. Int. Med. **85**: 545-666 (April) 1950.

8. Sprague, R. G.; Power, M. H.; Mason, H. L.; Albert, A.; Mathieson, D. R.; Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: Observations on the Physiologic Effects of Cortisone and ACTH in Man, Arch. Int. Med. **85**: 199-258 (Feb.) 1950.

arthritis under adequate, although not always complete, control for long periods. The size of the average maintenance dose roughly paralleled the severity of the disease.

In the nine patients who received cortisone orally from the beginning (group 2) the daily maintenance amounts required for continued satisfactory control were somewhat greater than those needed in comparable patients treated by intramuscular injection (table 2).

More direct comparisons of dosage requirements were possible in those patients of group 1 who had received cortisone by injection and who were transferred to orally administered cortisone without interrupting therapy; in these the maintenance doses by intramuscular injection had been established (table 1). Of the 14 patients in this group, one (C. B.) failed to show any therapeutic effect from oral use of cortisone. In the remaining 13 patients the maintenance dose required by mouth for equivalent antirheumatic control was approximately the same in two patients, one-fifth greater in three, about one-fourth greater in five and one-third greater in three. Although no constant dosage ratio could be established in these 13 patients on the basis of therapeutic response alone, it is apparent that larger doses, ranging from one-fifth to one-third more, may be needed when the hormone is given by mouth.

Differences in Therapeutic Response with Single and Divided Doses. — Results from cortisone given orally were definitely best when the drug was taken in divided doses with the time interval between doses fairly equally spaced. When the entire daily amount was given in a single dose each morning, part of the effect was dissipated by the following morning and the patients complained of aching, stiffness and joint tenderness on arising. Antirheumatic control was held uniformly throughout the 24-hour period, however, when the total dose was given in divided doses (for example, at breakfast, lunch, dinner and bedtime). Some patients preferred to take a smaller dose at bedtime, as they believed that this lessened the degree of mental stimulation during the night and allowed more restful sleep. For example, if the daily maintenance dose was 75 mg. they preferred to take a whole tablet (25 mg.) at breakfast, one-half tablet at noon, a whole tablet at dinner, and one-half tablet on retiring.

TABLE 2.—*Oral Use of Cortisone Acetate: Response of Group 2 Patients to Initial Large Suppressive Doses and to Maintenance Doses*

Patient	Sex	Duration of Disease (Mo.)	Severity of Disease	Form of Oral Medication		Onset of Initial Response (Hr.)	Degree of Response to Large Initial Suppressive Doses †	Average Maintenance Dose Required for Satisfactory Control (Mg.)
				Tablet	Suspension			
A. W.	F	38	Mod. sev.	X	..	8 *	Very marked	75.0
R. J.	M	27	Mod. sev.	X	..	5 *	Marked	100.0
M. D.	F	8	Mild	X	..	24	Very marked	50.0
P. S.	F	68	Mod.	X	..	24	Very marked	87.5
H. H.	M	72	Mod. sev.	..	X	7	Marked	75.0
F. S.	F	13	Mod. sev.	..	X	10	Very marked	62.5
M. R.	F	124	Sev.	..	X	12	Marked	75.0
F. H.	F	26	Mod. sev.	..	X	48	Marked	75.0
P. R.	F	120	Mod. sev.	..	X	6	Marked	62.5

* On the first day 200 mg. was given in a single dose.
† Improvement is graded as: very marked, 90 to 100 per cent improvement; marked, 75 to 90 per cent; moderate, 50 to 75 per cent; slight, less than 50 per cent, and unimproved.

Adverse Effects from Oral Administration.—Gastrointestinal symptoms or nonhormonal pharmacologic reactions have not resulted so far from the oral administration of cortisone acetate.

Although 18 of the 23 patients have taken cortisone by the oral route continuously for three months or slightly longer, the periods of observation have not been long enough to accumulate conclusive data regarding the incidence of adverse hormonal reactions. Signs of hypercorticalism in this series appeared in only one patient, a woman in whom slight facial hypertrichosis developed after she had received 100 mg. of the drug a day for two and one-half months. No instances of water retention, excessive nervousness or insomnia, acne, amenorrhea or other metabolic or clinical signs of hormonal excess have occurred to date.

Most patients agreed that for even control throughout the 24-hour period a dose at or near bedtime was needed. This observation suggests to us that in addition to its more rapid absorption the effects of cortisone may be dissipated sooner when it is administered by mouth. Symptomatic response apparently was not influenced by whether the drug was taken before, with, after or between meals.

Miscellaneous Observations.—Most patients believed that the degree of mental stimulation was less with oral use of cortisone even though the dose needed for the same therapeutic action was somewhat greater; they still "felt good," but they were not euphoric and did not experience insomnia or as much "nervous tension." Appetite stimulation was less than with parenteral administration, and increases in body weight were easier to control.

COMMENT

For chronic diseases such as rheumatoid arthritis the oral use of cortisone acetate has distinct advantages. It eliminates the discomfort from repeated intramuscular injections and makes the patient independent of others for his medicine. Those patients who had also

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received cortisone intramuscularly beforehand definitely preferred the oral route of administration. Most believed that when the drug was given in divided doses the rheumatic manifestations were more evenly controlled than when the drug was given by intramuscular injection. The less pronounced stimulation of mental activity and appetite is a practical advantage in the management of patients.

The most serious objection to the use of cortisone for chronic rheumatoid arthritis is the high incidence of hormonal side effects when administration is continued, especially in large doses, for extended periods. Serious trouble has been avoided until now by the strict regulations for its use imposed by the manufacturers and government agencies. The incidence of adverse reactions has been reduced substantially also by the use of smaller maintenance doses for prolonged control or by the employment of interrupted schedules of administration. But many more facts must be ascertained before this powerful hormone with its many physiological actions can be considered a safe therapeutic agent for general distribution and use. Now that the saline suspension of cortisone acetate has been placed on the market for sale, physicians must exert great caution in order to prevent its indiscriminate use. The knowledge that the hormone may be administered effectively by mouth should make physicians even more vigilant in preventing its abuse.

SUMMARY AND CONCLUSIONS

1. Cortisone acetate was given orally to 23 patients with chronic rheumatoid arthritis. In 22 of the 23 patients oral preparations were found to be highly effective in suppressing the activity of the disease and/or in maintaining control of the rheumatic manifestations.

2. The pattern of improvement with initial large suppressive doses of cortisone given by mouth was similar to that observed in patients who have received equivalent amounts of the hormone by intramuscular injection. In general, the antirheumatic effects were produced more rapidly and were dissipated more quickly with oral administration of the drug.

3. No constant ratio for the oral as compared to the intramuscular dose could be established. In 13 patients who received cortisone by both routes of administration, direct comparisons were made of the doses needed for maintenance of satisfactory antirheumatic control: the effective dose was approximately the same in two patients, but in the remaining 11 patients larger amounts, ranging from one-fifth to one-third more, were needed by mouth.

4. No gastrointestinal symptoms developed from the oral use of cortisone. Adverse hormonal side effects occurred in only one patient, but the number of cases studied was too small and the periods of observation were too short for conclusions to be drawn as to the safety of prolonged administration.

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CORTISONE AS AN ADJUNCT IN THE THERAPY OF ACUTE GOUT

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Briefly defined, clinical gout is a metabolic disorder of urate metabolism characterized by episode attacks of joint pains, with or without redness or swelling, in hyperuricemic persons. According to Harkavy [1] certain allergic factors may be involved in clinical gout. He states that there often is no relationship between the amount of uric acid in the blood and urine and the degree of arthritic involvement. Paroxysms of gout may occur with or without an elevated blood uric acid. The latter may be present between attacks when the patient is completely free of symptoms. Acutely affected joints have been found to be apparently free of urates, whereas certain symptomless joints may reveal extensive deposits of urates. There may be no constant relationship between the formation of resorption of tophi and acute attacks. Harkavy [1] believes that the concept that allergy may at times be a factor in the development of gouty attacks carries with it both theoretical and practical significance, particularly when prophylaxis and treatment are considered. The concept of an allergic factor in gout is not altogether recent but has not been clearly proved. Numerous precipitating factors have been considered. The dramatic subsidence of acute gout following the administration of pituitary adrenocorticotropic hormone (ACTH) lends speculative thought to this point, since many of the conditions responding to this hormone seem to have an allergic component.

According to Wolfson and Cohn [2] the adrenal cortical steroids are believed to be implicated both in the inherited susceptibility to gout and in the transition from asymptomatic hyperuricemia to clinical gout. They believe that inherited hyperuricemia and clinical gout are not synonymous. Clinical gout appears to be associated with the presence of a second endocrine disturbance characterized by a disturbed regulation of the rate of secretion of the 11-oxysteroids, i. e., those adrenal cortical steroids whose metabolic properties resemble those of cortisone (17-hydroxy-11-dehydrocorticosterone, or compound E). The mechanism by which clinical gout is precipitated in the hyperuricemic person is obviously complex. The reader is referred to the current literature regarding this phase of the subject. Of practical importance, however, is the fact that according to Thorn and associates [3] the decided increase in uric acid clearance and the remarkable

From the Division of Medicine, University of California School of Medicine.

1. Harkavy, J.: Allergic Factors in Gout, J. A. M. A. **139**: 75-80 (Jan. 8) 1949.

2. Wolfson, W. O., and Cohn, C.: The Role of the Pituitary Adrenocorticotropic Hormone (ACTH) and of Adrenal Cortical Steroid Hormones in the Pathologic Physiology and Experimental Therapeutics of Clinical Gout, in Mote, J. R.: Proceedings of the First Clinical ACTH Conference, Philadelphia, The Blakiston Company, 1950.

3. Thorn, G. W., and others: Medical Progress: The Clinical Usefulness of ACTH and Cortisone, New England J. Med. **242**: 783-793 (May 18); 824-834 (May 25); 865-872 (June 1) 1950.

reduction of inflammatory change in podagral joints represent clearcut indications for the use of pituitary adrenocorticotropic hormone.

It is well known that as the number of attacks of gout increases and as the chronicity of the disease progresses the majority of patients with this metabolic disorder eventually manifest renal damage.[4] This probably interferes with the excretion of urates and renders the gouty attacks of the patient less susceptible to the usual measures of treatment, i. e., low purine diet, colchicine and salicylates. The picture then becomes that of chronic gout, which may progress to the tophaceous stage, as compared to the so-called interval gout with acute exacerbations. In some cases relief is exceedingly difficult to achieve, so that it was only natural that the pituitary adrenocorticotropic hormone should have been tried in this as well as in other rheumatic conditions as soon as it became available. As it is now known, the relief in many cases is both rapid and dramatic.

The literature concerning the treatment of gout with pituitary adrenocorticotropic hormone at the time of this report has been thoroughly reviewed and includes articles published by Thorn and co-workers,[5] Hench and associates,[5] Boland [6] and Gutman and Yü.[7] The last-mentioned workers [7] believe that the hormone acts as an uricosuric agent in gout and that it is a useful agent in the therapy of acute gout. In their opinion it is neither feasible nor desirable to use it in the prevention and treatment of chronic tophaceous gout. I am of the opinion, however, that further studies may eventually demonstrate its value in preventing or at least delaying the occurrence of tophaceous gout.

Although pituitary adrenocorticotropic hormone and cortisone produce similar effects in the body, they are obviously different substances structurally. The former is an adrenocorticotropic hormone derived from hog pituitary glands. The latter is prepared by partial synthesis from bile acids. Pituitary adrenocorticotropic hormone produces its therapeutic effects, according to Thorn and others,[3] by stimulating the adrenal cortex to increase the secretion of adrenal steroids including cortisone and closely related compounds. The effectiveness of the pituitary hormone and cortisone appears to vary directly with the level of circulating adrenocortical hormones obtained and with the responsiveness of the tissues on which they act. It appears, according to Thorn and associates,[3] that a given quantity of pituitary adrenocorticotropic hormone may elicit a variable increase in adrenal steroid output, depending on the state of activity of the adrenal cortex at the time therapy is instituted. Thus, a quiescent gland may respond minimally to a standard dose of the hormone, whereas an exceedingly active gland may show a tremendous, absolute increase in output. A limiting factor, therefore, in the response to pituitary adrenocorticotropic hormone is the capacity of the adrenal cortex to react to stimulation. If this is so, a definite given dose of cortisone should be a more dependable therapeutic agent in the treatment of acute exacerbations of gout than is pituitary adrenocorticotropic hormone. At this time, a perusal of the current literature by investigators closest to this field reveals the use of cortisone in acute gout in only two cases.[6] I have treated a number of patients with gout in the practice of medicine in the past 20 years but have never witnessed such dramatic relief, subjectively and objectively, as that described in the following case report, subsequent to the administration of cortisone.[8]

4. Brown, J., and Mallory, G. K.: Renal Changes in Gout, New England J. Med. **243**: 325-329 (Aug. 31) 1950.

5. Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: Effects of Cortisone Acetate and Pituitary ACTH on Rheumatoid Arthritis, Rheumatic Fever and Certain Other Conditions: A Study in Clinical Physiology, Arch. Int. Med. **85**: 545-666 (April) 1950.

6. Boland, E. W.: The Effects of Cortisone and Adrenocorticotropic Hormone (ACTH) on Certain Rheumatic Diseases, California Med. **72**: 405-414 (June) 1950.

7. Gutman, A. B., and Yü, T. F.: Effects of Adrenocorticotropic Hormone (ACTH) in Gout, Am. J. Med. **9**: 24-30 (July) 1950.

8. Cortone® (cortisone acetate, Merck).

REPORT OF CASE

History.—G. C., a married man aged 50, on Aug. 21, 1947 complained of a burning sensation in the epigastrium, usually awakening him around 5 o'clock in the morning. This symptom had been of about 10 days' duration and was relieved by induced vomiting. He stated that he had had no abdominal discomfort during the day, nor had there been any spontaneous nausea or vomiting. He was aware of no dietary idiosyncrasies and had not noticed black or tarry stools. He had lost no weight, and his diet had remained unchanged for many years. His occupation was that of an executive in an investment firm, and as such he was subject to a good deal of mental stress and strain. He stated that he had had a physical examination in 1946, at which time his weight was 162 pounds (73.5 Kg.), height 5 feet 8½ inches (174 cm.) and blood pressure 158/108 mm. of mercury. He was told that his prostate was twice normal size, but he denied any urinary difficulties other than nocturia once nightly. There was no diurnal urinary frequency. Reaction of the blood to Wassermann and Kahn tests on June 5, 1946 was negative, and chest roentgenogram on April 19, 1946 was reported as revealing essentially normal conditions. The patient seemed to be more concerned about the elevation of his blood pressure than about his gastrointestinal symptoms; he believed that the former warranted further observation. A thorough medical survey was advised. The past history was not remarkable. He had lived in California all his life. During childhood he had measles, mumps, whooping cough and diphtheria. A tonsillectomy was performed in 1916, and he had influenza in 1918. In 1938 he fractured several ribs and his nose in an auto accident. His habits were moderate as a rule, with occasional episodes of excessive alcoholic consumption on social occasions. During the past few years there had been a tendency to gain weight. For many years he had had seasonal hay fever, which had always been treated symptomatically. The family history was not contributory, except that a brother was said to have died at the age of 6 of Bright's disease and a sister, 54 years of age, had mild diabetes and hypertension.

Physical Examination.—The patient was a well developed and well nourished, healthy appearing man who weighed 173½ pounds (78.7 Kg.). The pulse rate was 90 per minute, the rhythm regular; blood pressure in the left arm was 205/120 and in the right arm 200/125. The skin was normal except that the lower two thirds of the legs showed an extensive light brown pigmentation. The skin of these areas was crinkly, atrophic and parchment-like. There was moderate pitting edema of the shins and ankles. These conditions were believed to be due to varicose veins. It was not possible to

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perform a satisfactory funduscopic examination at this time because of the smallness of the pupils. The bridge of the nose was somewhat depressed as a result of the nasal fracture in 1938. The teeth were in good repair. The posterior nasopharynx was hyperemic, and there was slight recurrence of tonsillar tissue bilaterally. The chest was clear, and there was no cardiac enlargement. Cardiac murmurs were not heard, and the heart sounds were normal in quality. There was no evidence of peripheral arterial disease. Examination of the abdomen did not reveal masses, scars or tenderness. The deep and superficial reflexes were normal. The prostate gland was approximately twice normal size. Examination of the blood revealed hemoglobin 108 per cent (15.7 Gm.); red blood cells 5,550,000, and white blood cells 6,150, with a differential of polymorphonuclear leukocytes 65 per cent, lymphocytes 21 per cent, monocytes 9 per cent and basophils 5 per cent, and a smear was normal. Urinalysis showed a low specific gravity on two occasions, 1.007 and 1.006, but no albumin or sugar and no abnormalities in the sediment. The Kahn and Kolmer tests were negative. The sedimentation rate (Wintrobe) was 10 mm. in one hour. A fasting blood nonprotein nitrogen determination was 35.7 mg. per 100 cc. The stool was negative for occult blood. A histamine gastric test meal showed no free hydrochloric acid after histamine. An electrocardiogram revealed normal conditions. Radiological studies of the upper part of the gastrointestinal tract were entirely negative except for decided spasm of the antrum. Fluoroscopy of the chest showed no abnormalities.

Treatment and Course.—In view of the preceding observations the patient was considered to have seasonal hay fever and essential hypertension without signs of renal involvement. The gastrointestinal symptoms were considered to be psychosomatic in nature and were treated symptomatically. He was seen at irregular intervals for minor complaints until Sept. 30, 1949, when he complained of visual impairment in the right eye. His oculist stated that a funduscopic examination showed a patch of choroiditis near the macula in the right eye, but the visual fields were not tested. It was the opinion of the oculist that this was not a hypertensive retinopathy, although there were definite early arterial changes, Keith-Wagner, grade 2. Several devitalized teeth were removed, and the vision in the right eye improved soon thereafter. On March 11, 1950 the patient's blood pressure was 180/140, the pulse rate 85, the rhythm regular and the heart and lungs normal. Examination of the fundi revealed some residual evidence of the former choroiditis in the right eye. The urine was normal except for a faint trace of albumin. On April 21, 1950 the patient was hospitalized because of nausea and vertigo of a week's duration and what at that time appeared to be auditory hallucinations. Psychiatric consultation failed to reveal any major psychosis. It was considered that the symptoms were explainable on the basis of an anxiety tension state associated with unpleasant situational factors with one of the patient's business partners. An electrocardiogram now showed early evidence of left ventricular hypertrophy. Reaction of the blood to the Kahn test was negative. The hemoglobin was 97 per cent (16.0 Gm.), the red blood cell count 5,500,000, and the white blood cells 6,400, with a differential count of polymorphonuclear leukocytes 66 per cent, lymphocytes 23 per cent, monocytes 8 per cent, basophils 2 per cent and eosinophils 1 per cent. The fasting blood creatinine level was 1.42 mg. and the blood urea nitrogen 15 mg. per 100 cc. Although the corrected sedimentation rate was 28 mm. in one hour, the patient was afebrile. The urine had a specific gravity of 1.011, albumin (2 plus), no glucose, an occasional white blood cell and three to six red blood cells per high power field, and an occasional hyaline cast. After an intravenous injection of phenolsulphonphthalein a renal function test was performed, which showed a 10 per cent excretion of dye in the first 15 minutes after its administration, 10 per cent excretion ½ hour after its administration and 15 per cent in the next ½ hour, a total excretion of 35 per cent of dye in one hour. In view of the above evidence of early renal impairment and the sustained hypertension, the advisability of bilateral dorsolumbar sympathectomy was discussed with the patient. Both he and his wife, however, refused to consider this procedure.

Diagnosis of Condition as Gout.—On June 16, 1950 he reported that his right first metatarsal phalangeal joint was painful. Examination showed that the skin overlying this joint was red, tense and swollen and that the area was extremely painful subjectively and on pressure. He was able to walk only with great difficulty. Further questioning elicited the fact that these symptoms actually began, to a mild degree, while he was in the hospital in April 1950, but he did not mention them at the time nor were there objective changes noted during the physical examination. However, about June 5, 1950 they became severe enough to interfere with his daily activities. The patient was asked whether he had previously had similar symptoms, and he stated that he had had pain in both the right and the left first metatarsal phalangeal joints about every year and a half for the preceding 15 years, the symptoms usually lasting a day or two and being of a minor nature. This is an interesting example of how a major disorder may be overlooked, despite thorough history-taking. He was asked why he did not mention this complaint in 1947. He stated he had forgotten about these symptoms but he had been told in 1935 by a physician that his symptoms were suggestive of gout. This physician stated that "he hoped he did have gout as he had never seen a case" but finally informed the patient that his condition was due to "neuralgia." Thus reassured, during the following 15 years he was not concerned about his mild symptoms, which were always relieved in a day or so by application of heat and by small doses of salicylates, such as aspirin (acetylsalicylic acid). On June 16, 1950 his blood pressure was 240/170, his weight was 162½ pounds (73.7 Kg.), and there were no tophi to be seen. The blood uric acid was 6.7 mg. per 100 cc. (normal 2.5 to 5.5 mg.). Roentgenograms of the involved foot showed changes consistent with, but not characteristic of, gout; they were more typical of hypertrophic arthritis than of gout, as is often the case in this condition. The patient was advised to follow a purine-free diet, take 40 grains (2.59 Gm.) of sodium salicylate (enteric coated) daily, in divided doses, and 1/120 grain (0.5 mg.) colchicine every two hours, night and day, until toxic symptoms from the latter developed, assuming that the development of such symptoms would be followed by some relief. After seven doses of colchicine there was only slight relief of his distress; nausea and vomiting ensued, and the patient refused to take any more of the drug. The dietetic and salicylate regimen was continued until July 8, 1950, when pain in the right foot became unbearable.

Cortisone Therapy.—Since the patient refused to resume colchicine therapy, the use of cortisone was suggested. Treatment with cortisone in patients with hypertension has not resulted in any significant elevation of the blood pressure.[3] Prior to the administration of cortisone the following fasting blood chemical values were noted: the uric acid was 13.9 mg. (normal 2 to 6 mg.), the urea nitrogen 24 mg. (normal 10 to 20 mg.) and the creatinine 2.1 mg. (normal 0.9 to 2.1 mg.), per 100 cc. The blood pressure at this time was 240/180. Relief followed the intramuscular administration of 100 mg. of cortisone in less than eight hours. Not only was the subjective relief dramatic and complete, but the right first metatarsal phalangeal joint appeared normal as compared to the left. The blood pressure the following day was 220/160. The patient was then given 100 mg. of cortisone daily for the next two days, although this additional dosage probably was unnecessary. On July 13, 1950 he complained of a mild recurrence of distress in the right foot, but objectively there were no changes. The blood uric acid was 4.4 mg. per 100 cc. This recurrence may have been due to 11-oxysteroid lack provoked by the withdrawal of cortisone,

as has been described in cases of gout treated with pituitary adrenocorticotropic hormone.[9] The patient was again given 100 mg. of cortisone intramuscularly each day for three days; colchicine, 1/120 grain three times daily, was resumed in addition to the salicylates and low purine diet. Relief was just as immediate and dramatic as it was the first time that cortisone was administered, and it has continued so to date. A small dose of sodium salicylate, 20 grains (1.29 Gm.) daily, a low purine diet and 1/120 grain of colchicine twice daily have kept this patient comfortable to date.

COMMENT

The small maintenance dose of colchicine was prescribed because recent studies indicated that this drug in small amounts seems to prevent the occurrence of 11-oxysteroid lack following the withdrawal of pituitary adrenocorticotropic hormone in gout. In an excellent later study by Wolfson and associates [10] on gout and its treament with pituitary adrenocorticotropic hormone and colchicine, it was shown that the mechanism by which colchicine relieves gout and the reason for its specific action remain entirely unknown. Although therapeutic doses of colchicine occasionally seem to release some adrenocorticotropic hormone, the amount is extremely small; yet the fact remains that colchicine has a synergistic effect when used with pituitary adrenocorticotropic hormone or cortisone. Nontoxic maintenance doses of colchicine seem to prolong remissions of acute gout after the withdrawal of pituitary adrenocorticotropic hormone or cortisone. In this particular case the recurrence or subsidence of this patient's symptoms could well be spontaneous, but it would seem that the reason for his persistent failure to improve without cortisone might be based on the renal damage which was not present in the earlier years of his illness and which was now preventing the excretion of urates through the kidneys as had taken place in the past.

SUMMARY

A case of acute interval gout is reported in which the relief following the administration of cortisone was both rapid and dramatic. Cortisone was not administered in this case until the usual methods of treatment had failed. This case is reported as confirmatory evidence of similar instances in which it has been demonstrated that the use of pituitary adrenocorticotropic hormone (ACTH) and colchicine has proved valuable in the termination of an acute attack of interval gout. It is suggested that cortisone is a more efficacious therapeutic agent in such cases than pituitary adrenocorticotropic hormone [11] and that it may prove in the future to be an important means of preventing tophaceous gout.

9. Hellman, L.: Production of Acute Gouty Arthritis by Adrenocorticotropin, Science **109**: 208-281 (March 18) 1949.

10. Wolfson, W. Q.; Hunt, H. D.; Cohn, C.; Robinson, M. D., and Duff, I. F.: ACTH and Colchicine in the Clinical Treatment of Acute Gouty Arthritis: Physiological Considerations and Review of Therapeutic Results in 51 Attacks, J. Michigan M. Soc. **49**: 1058-1064 (Sept.) 1950.

11. Samuels, L. T.; Nelson, D. H., and Reich, H.: The Effect of ACTH upon the Level of 17-Hydroxycorticosterone in the Adrenal Blood Vein of Dogs, J. Clin. Endocrinol. **10**: 810 (July) 1950. Thorn and others.[5]

1. Aaron, A. H.; Lipp, W. F., and Milch, E.: Newer Aspects of Peptic Ulcer Therapy, J. A. M. A. **139**: 514-518 (Feb. 19) 1949.

MANAGEMENT OF MASSIVE HEMORRHAGE FROM GASTRODUODENAL ULCERATION

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Massive hemorrhage is defined as massive continuing hemorrhage into the upper gastrointestinal tract with an exhibition of the classic picture of collapse: pallor, sweating, air hunger, hypotension, tachycardia, acute anemia, diminished blood volume and reduced hematocrit. (It should be recognized that the values of the laboratory determinations do not always furnish an accurate index of the severity of the bleeding. The red blood cell count is usually below 2,500,000 per cubic millimeter. However, in several instances in our series death occurred in patients with erythrocyte counts of more than 3,000,000 per cubic millimeter.)

We believe that in the majority of instances this usually critical state will respond to intensive medical treatment consisting of massive and continuous multiple transfusions, oxygen and opiates, that in a certain small group of patients surgical intervention with gastric resection will be required, and that members of this group can be rather readily determined through their failure to respond to transfusion.[1] The strength of this position is enhanced by its general applicability throughout the country. In this communication no attempt will be made to discuss the question of elective, definitive surgical procedures for patients who have had one or more bouts of hemorrhage.

During the past several decades there have been innumerable reports concerning the management of massive hemorrhage from peptic gastroduodenal ulceration. Many of these have supported medical treatment, while some have favored early surgical intervention. The abundance of these reports in itself indicates the confusion that continues to surround this problem. For years the attitude has fluctuated between the extremes of medical and surgical treatment. Of course this rather cyclic fluctuation implies continuing dissatisfaction with concurrent mortality figures.

It is now, as it has been in the past, our contention that the persistent controversy between medical and surgical forms of treatment not only is unnecessary but is misleading to the practitioner. The usefulness of both forms of therapy should be apparent to anyone called on to treat large groups of bleeding patients. Although it is well known that the majority of patients with hemorrhage will respond to conservative medical

Dr. James D. MacCallum assisted in the analysis of the clinical material.

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treatment, a certain number will not survive who have lesions that are susceptible to surgical treatment. On the other hand, because of the relatively high mortality rate, even in competent hands with highly specialized facilities, of routine early gastric resection, this operation cannot be considered the treatment of choice in massive hemorrhage.

It is acknowledged that operative intervention requires a team of six to eight highly trained persons, painstaking preoperative preparation and postoperative care, including laboratory studies, a skilled surgeon, resident and nursing staff and adequate blood. And in the majority of instances this intensely coordinated activity will take place during the night when bleeding so frequently occurs. Furthermore, acceptance of the concept of early gastric resection requires the security of the correct diagnosis. Although the probability of peptic ulcer is great (approximately 80 to 85 per cent of patients with massive hemorrhage) and the diagnosis is usually evident, there are other sources of bleeding in which emergency operative procedures may not be indicated. Moreover, it is not generally appreciated that successful surgical intervention requires considerable surgical treatment, such as the removal of the ulcer (the point of bleeding) as part of the gastric resection, and this can often be technically difficult and sometimes impossible. In these instances, in addition to the resection one must be sure that the pancreaticoduodenal artery is ligated. It is at once obvious that such a service is not generally available. Nevertheless it is to be hoped that studies, such as those of Stewart,[2] will be continued because they do much to illuminate the problem of the treatment of massive hemorrhage. With more experience it is likely that a reduction in surgical mortality rates will occur, thus permitting the operation of gastric resection to be more widely used as a relatively safe method to attack the bleeding at its source. No one will deny that local control with mechanical measures is the most efficient means of arresting hemorrhage in whatever portion of the body it may occur.

In view of the relative success of conservative medical management and because of the definite need of gastric resection in certain patients who fail to respond to medical therapy, it is our firm belief that the treatment must be individualized to fit the special needs of the patient. The many reviews that have appeared in recent years reporting mortality figures cited as evidence favoring one method of treatment over the other and with generalizations and conclusions drawn from series of patients are grossly inadequate when one is confronted with a patient with massive hemorrhage. The individual patient remains an individual problem in management, in spite of classifications and criteria. This is as it should be, for the fundamental weakness in the study of any large series of patients is the failure to take into consideration the extremely variable and the frequently unpredictable reaction of individual patients to hemorrhage, and this is due in great part to the rate of blood loss. Unfortunately, the reports in the literature cannot be compared largely because there is lack of uniformity in the classification of bleeding patients and because the interpretation of the term massive hemorrhage varies from group to group. There is little doubt that it is frequently difficult if not impossible to segregate patients on the basis of any selected criteria. The same data are susceptible to various interpretations by different examiners, and even unintentional statistical manipulation may occur, resulting in unreliable analysis. We are convinced that it is this variation in the inclusion and exclusion of cases, and not the particular method of therapy employed, that has led to the discrepancies in mortality figures, which range from 2.5 to 40 per cent.

On the basis of our own experience, which is in keeping with that of others, certain definite observations which possess prognostic value can be reemphasized: first, massive hemorrhage in older age groups is associated with a higher mortality; second, hematemesis has more ominous significance than melena, for it usually indicates sudden and massive expulsion of blood into the upper gastrointestinal tract; third, recurrent hemorrhage while the patient is in the hospital under observation is a serious event, and fourth, the prognosis is more serious if any of several additional diseases (portal cirrhosis, essential hypertension or cardiac failure) is present. Again it should be emphasized that to us the term massive hemorrhage means massive continuing bleeding with an exhibition of the classic picture of collapse : pallor, sweating, air hunger, hypotension, tachycardia, acute anemia, reduced hematocrit and diminished blood volume.

RESULTS OF MEDICAL MANAGEMENT

From the years 1938 to 1949 there were 274 patients admitted to the Buffalo General Hospital with bleeding peptic ulcer of varying degrees.[3] The difficulties of classifying this group of patients were at once apparent, in spite of the establishment of criteria having to do with the duration of bleeding, the clinical picture of shock, the level of the blood pressure, the red blood cell count and the hematocrit determination. Of the 274 patients there were 101 who could be reasonably considered to have massive hemorrhage of less than one week's duration, although even this attempt at segregation may be open to question. In this group of 101 patients conservative medical management was employed in all instances, with a number of internists participating and without a prescribed formula of therapy. Fifteen deaths occurred, all in men, a mortality rate of 14.8 per cent.

The study can be subdivided into two 6 year periods (table 1): In the first period (1938-1943) there were 40 cases with 10 deaths, a mortality rate of 25 per cent; in the second period (1944-1949) there were 61 cases with five deaths, a mortality rate of 8.2 per

2. Stewart, J. D.; Massover, A. J.; Potter, W. H., and Schaer, S. M.: Massive Hemorrhage from Gastroduodenal Ulcer, Surgery 24: 239-245 (Aug.) 1948.

3. MacCallum, J. D.: Proc. Staff Meet., Buffalo General Hospital, unpublished data.

cent. A brief analysis of the deaths is shown in table 2. It will be noted that in the first period (1938-1943), seven of the 10 patients were over 50 years of age, and of these 6 were aged 60 or more. Three patients had associated diseases (two portal cirrhosis and one pneumonia); one man collapsed and died suddenly after radiographic examination of the stomach and duodenum. However, seven in all died (including three patients under 50 years of age) of hemorrhage alone.

In the second period (1944-1949), all five patients who died were over 50 years of age, and of these four were over 60 and three over 70 years of age. Three of these five patients had additional diseases (one hypertension, one portal cirrhosis and one advanced generalized arteriosclerosis with peripheral vascular occlusion and gangrene). One of the two patients dying

TABLE 1.—*Results of Medical Management in 101 Cases of Massive Hemorrhage (1938-1949)*

Period	No.	Deaths	Mortality, %
1938-1943	40	10	25
1944-1949	61	5	8.2
Total	101	15	14.8

TABLE 2.—*Analysis of Fifteen Deaths Occurring in 101 Cases of Massive Hemorrhage*

	Case	Age	Sex	Remarks
1938 to 1943	1	74	M	Improving, sudden exsanguination
	2	74	M	Died within 24 hr.
	3	66	M	.....
	4	62	M	Portal cirrhosis
	5	61	M	Portal cirrhosis, died in 3 hr.
	6	60	M	Death followed roentgenologic examination
	7	51	M	Pneumonia
	8	49	M	.....
	9	48	M	.....
	10	31	M	.....
1944 to 1949	11	78	M	Hypertension, nephrosclerosis
	12	74	M	Arteriosclerosis, peripheral vascular occlusion
	13	71	M	.....
	14	69	M	Sudden exsanguination, while under observation
	15	51	M	Portal cirrhosis

of bleeding alone had a single sudden massive hemorrhage while in the hospital for treatment of intractable ulcer.

It is evident that when adequate medical therapy is given it is less usual for patients to die of hemorrhage alone, and frequently there is a coexisting disease. The likelihood of associated disease or of malnutrition or deficiency states is increased in municipal institutions, which draw so frequently on a segment of the population exposed to hardship and various stresses and strains related to unsatisfactory environment.

The chief factor, we believe, that will explain the decrease in the mortality rate from 25 to 8.2 per cent is the more liberal use of transfusions. Of course it is reasonable to assume that the patients in the later period had the advantages of the application of more recent medical knowledge, closer observation and the wider use of laboratory studies. If the mortality rate for patients with hemorrhage who are under modern medical management is between 8 and 9 per cent, it is difficult to justify abandonment of such a successful form of therapy. It is reasonable to expect that deaths will continue to occur in patients of advanced years and with coexisting diseases. Yet it is obvious that certain of the deaths could have been and can be prevented by radical surgical intervention with gastric resection. It has already been pointed out that many of the suggested criteria for operative intervention are inadequate and difficult to apply in the individual case. However, there is one criterion that is not only relatively reliable but also available for general application, and that is the "test of transfusion."

TEST OF TRANSFUSION

The patient who has massive continuing hemorrhage with the classic picture of collapse should immediately have multiple transfusions in addition to the usual supportive therapy (oxygen, nasogastric drainage and opiates), with as much as 2,000 cc. of blood being administered in an hour if necessary. At the end of three hours of this treatment, if there is no appreciable clinical improvement in the patient as indicated by a rise in blood pressure, reduction in pulse rate and disappearance of air hunger, the patient is a candidate for immediate operative intervention, inasmuch as it is apparent that he is losing blood as rapidly as it is being replaced. Of course if this persists for a few more hours the shock state will become irreversible, so that resection will not save the patient.

However, if at the end of three hours clinical improvement is manifested, the treatment is continued and at the end of six hours blood replacement is interrupted and the patient carefully watched for further evidence of bleeding. If the patient once again starts to bleed massively, transfusions are again inaugurated and surgical operation is performed at once. However, if the patient does not show evidence of massive bleeding after discontinuance of transfusion, the medical plan of treatment is continued.

Under this regimen as much as 5 liters (5,000 cc.) of blood may be administered in the six hour period. In the past year four patients, all in older age groups, have had successful gastric resection after having failed to meet the transfusion test.

SUMMARY AND CONCLUSIONS

1. The continuing controversy between proponents of medical and surgical forms of treatment of massive hemorrhage is both unnecessary and the cause of real confusion.

2. The majority of patients with acute massive hemorrhage will respond to medical therapy which emphasizes the liberal use of blood.

3. It is more usual for death to occur in patients of advanced years and those having associated diseases.

4. A method of selection of those patients requiring gastric resection, based on the response to transfusion, is outlined.

5. This approach to the problem of massive hemorrhage possesses the advantage of general applicability.

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MASSIVE UPPER DIGESTIVE TRACT HEMORRHAGE OF UNDETERMINED ORIGIN

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and
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In a previous communication [1] one of us (I. R. J.) analyzed 60 cases of massive upper digestive tract hemorrhage of unexplained origin. Suggestions were made for earlier and more intensive studies of such patients in order to reduce the number of diagnoses of bleeding due to unknown causes, which at the Boston City Hospital was then as high as 9 per cent. Schiff [2] reported the incidence of such bleeding as 26.4 per cent; Thompson and associates,[3] 2 per cent; Crohn, Marshak and Galinsky,[4] 20 per cent, and Costello,[5] 1.3 per cent. In accord with our previous suggestions, another group [6] at the Boston City Hospital recently has been intensively studying on admission patients bleeding from the digestive tract. Their report is that 5 per cent of the cases still remain unexplained. But when the frequency of hospital admissions for severe hemorrhage of the upper part of the digestive tract is considered, even 5 per cent is too high.

In our desire to learn the ultimate diagnosis in cases of massive upper digestive tract hemorrhage, some of which remained unexplained after several episodes, we observed a group of 27 patients for two to 12 years. At the time of this writing, we know of no similar studies reported in the literature, although many experienced physicians undoubtedly have observed such cases, some for even longer periods than we did. The analysis of data on these 27 patients constitutes the material for this presentation.

From First and Third (Tufts) Medical Services, Boston City Hospital.
Read before the Section on Gastro-Enterology and Proctology at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 28, 1950.

ANALYSIS OF MATERIAL

The 27 patients observed for two to 12 years had 66 upper digestive tract hemorrhages (table 1). Of these, 14 occurred prior to the time when the patients came to our attention. Fifty-two hemorrhages were observed in this group of patients (table 2) and are analyzed here. All patients were hospitalized (some repeatedly), studied while in the hospital and followed up.

The severity of the hemorrhages varied from case to case, but each patient had at least one massive bleeding episode. In 27 instances there were tarry stools only; in 25 hematemesis was followed by melena. The amount of blood lost was estimated by the hemoglobin, red blood corpuscles, blood pressure and pulse rate. The hemoglobin varied from 3.5 to 9 Gm. and the red blood cell count from 1,600,000 to 3,000,000. The pulse rate was elevated and the blood pressure was low in all cases. Some patients were admitted to the hospital in shock. Twelve patients had one massive hemorrhage each, 10 had two episodes each, one had three, three had four and one had five.

TABLE 1.—*Pertinent Data on the Patients Who Form the Basis of This Study*

Case	Name	Age	Sex	First Seen	Number of Hemorrhages	Surgery	Ultimate Diagnosis
1	A. C.	33	M	1938	1	None	Hypertrophic gastritis
2	J. B.	35	M	1938	1	None	Unexplained
3	I. F.	33	M	1939	4	Subtotal gastrectomy	Gastric ulcer
4	L. C.	36	F	1939	1	None	Unexplained
5	S. B.	47	F	1941	2	None	Hiatus hernia
6	J. B.	59	M	1942	1	None	Unexplained
7	M. G.	23	F	1942	3	Resection	Hemangioma of jejunum
8	A. H.	45	M	1942	2	None	Unexplained
9	B. S.	52	M	1943	5	Exploratory	Cancer of stomach
10	S. G.	31	M	1943	2	Subtotal gastrectomy	Duodenal ulcer
11	L. B.	57	F	1944	2	None	Unexplained
12	J. O'D.	48	M	1945	1	Subtotal gastrectomy	Gastric ulcer
13	F. E.	62	F	1945	2	Exploration	Unexplained
14	C. M.	48	F	1946	1	None	Hypertrophic gastritis
15	S. Z.	39	M	1946	2	None	Unexplained
16	G. S.	23	M	1946	1	None	Unexplained
17	L. S.	47	F	1946	2	Subtotal gastrectomy	Duodenal ulcer
18	M. Z.	62	F	1946	1	None	Unexplained
19	B. L.	45	M	1946	1	None	Unexplained
20	M. S.	57	M	1946	2	4 explorations	Unexplained
21	M. W.	62	M	1947	1	None	Unexplained
22	R. W.	53	F	1947	4	Exploration	Unexplained
23	J. M.	43	M	1947	4	Exploration	Cancer of liver
24	J. G.	13	F	1947	2	None	Unexplained
25	M. C.	47	F	1947	1	None	Unexplained
26	A. G.	65	F	1947	2	None	Unexplained
27	R. R.	45	M	1947	1	None	Cirrhosis of liver

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There were 15 males and 12 females, all white. The ages of the patients when first seen ranged between 13 and 65 years (table 3). A girl aged 13 was the only patient in the second decade. There were two patients between 20 and 29 years of age, six between 30 and 39, nine between 40 and 49, five between 50 and 59 and four between 60 and 65. The average age of the male patients was 43.5 years and of the females was 46.5. Three of the four patients in the seventh decade were females.

TABLE 2.—*Number of Hemorrhages Observed*

Hemorrhages	No. of Patients
1	12
2	10
3	1
4	3
5	1
Total 52	27

All the patients, with the exception of one, were treated medically on the first admission. The one exception is a patient who because of uncontrollable hemorrhages underwent operation on the third hospital day.

Despite careful studies, the cause of the hemorrhages remained unexplained after the first hospital admission. These studies included, in addition to a clinical history and repeated thorough physical examinations, at least one and in some cases two complete gastrointestinal roentgenologic series. Other studies included relevant laboratory tests, such as gastric analysis, stool examinations, multiple liver function tests and complete blood studies. In some patients gastroscopy and esophagoscopy were performed. Unfortunately, as suggested in a previous communication,[1] few of the patients were studied soon enough after their original hemorrhage. At the time of discharge from the first hospital admission, various diagnoses were made. In eight cases the diagnosis was gastrointestinal hemorrhage of unexplained origin. The diagnosis was peptic ulcer (not confirmed by roentgenograms) in five cases, question of peptic ulcer in four, chronic gastritis in seven and probable esophageal varices in three. However, a careful review of the clinical records does not present sufficient evidence to justify such diagnoses.

TABLE 3.—*Age Distribution of the Twenty-Seven Patients*

Decades	No. of Patients
2d	1
3d	2
4th	6
5th	9
6th	5
7th	4

After their discharge from the hospital these patients were carefully followed by us (table 4). Throughout the period of observation repeated search for new evidence on the cause of the prior hemorrhage or hemorrhages was the keynote of these studies. The histories were reviewed for new symptoms and for more careful evaluation of the old ones. Many new examinations were made, including physical, roentgenologic and endoscopic. Repeated varied laboratory tests supplemented those done after the acute hemorrhagic episodes. During the course of our study 25 additional acute hemorrhages occurred in 15 patients, who were readmitted to the hospital for treatment and reevaluation.

Seventeen patients were treated medically. Of these, 11 patients had a single hemorrhage each and six had two hemorrhages each. During and immediately after the first massive hemorrhage its cause remained unexplained. An eventual diagnosis as to the source of bleeding was made in four patients. Two patients had hypertrophic gastritis with multiple fissures, as diagnosed by gastroscopy. Each had one hemorrhage and rather insignificant symptoms involving the upper part of the digestive tract before and after this episode. In one instance a diagnosis of cirrhosis of the liver was made two years after the patient had the hemorrhage. During the course of our observation he manifested a palpable hard liver, spider angiomas over the thorax and hepatic insufficiency as determined by repeated serial liver function tests. In another patient with two hemorrhages in four years and otherwise nondescript digestive symptoms, a small reducible hiatus hernia was demonstrated on three subsequent gastrointestinal roentgen series.

TABLE 4.—*Ultimate Diagnosis After Two to Twelve Years of Follow-Up*

Pathologic Condition	No. of Patients
Clinical diagnosis	
Duodenal ulcer	2
Gastric ulcer	1
Hypertrophic gastritis	2
Cancer of stomach	1
Cancer of liver	1
Cirrhosis of liver	1
Diaphragmatic hernia	1
Diagnosis made at exploration	
Hemangioma of jejunum	1
Gastric ulcer	1
Clinically undetermined	16

In 13 patients who had one or two upper digestive tract hemorrhages and were treated medically the cause remained unexplained for two to 12 years. To four of the five patients with two hemorrhages exploratory laparotomies were suggested, but they refused to permit operation.

The reasons for the failure to make a definitive diagnosis of the source of the bleeding were as follows: Eight patients with a single severe upper digestive tract hemorrhage had either no or equivocal digestive symptoms before and after the bleeding. The physical examinations while the patients were in the hospital were noncontributory, showing only the usual signs of acute blood loss and unrelated accidental observations. The laboratory studies, roentgen examinations and other studies gave negative or equivocal data at that time as well as subsequently when they were reevaluated. These patients remained well for two to 12 years under our observation. Five patients had two episodes of massive bleeding each. The intervals between the two episodes varied from eight months to two years and our follow-up studies from two to seven years. In this group, too, a diagnosis of the etiological basis of the hemorrhages was impossible because symptoms of the patients were either absent or minimal, bizarre or indefinite and because results of repeated studies were negative, equivocal or noncon-

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tributory. There were no deaths in the medically treated cases.

Ten patients have undergone 13 operations. The patients operated on include five in whom intensive studies revealed the source of bleeding, namely, a duodenal ulcer in two patients, an ulcer of the lesser curvature of the stomach in the third, a cancer of the stomach in the fourth and biliary tract cancer in the fifth. The three patients with demonstrated ulcers had subtotal gastrectomies, one 4 days after his second hemorrhage, another 10 days after onset of his second bleeding episode and one 6 weeks after his third acute hemorrhage. The fourth and fifth patients in this group are described in the case reports (cases 9 and 23). Three patients underwent surgical exploration, but no lesion was found. One of them (case 20), despite four exploratory operations and intensive clinical studies, did not have the cause of hemorrhage determined. In two patients definite lesions explaining the recent hemorrhages were found. One patient, explored after her third exsanguinating hemorrhage, had a hemangioma of the jejunum. It was resected, and in the two years since then further hemorrhages have not occurred. In the second patient, a posterior wall prepyloric ulcer was found at operation and a subtotal gastrectomy performed.

Six of the 10 patients made an uneventful recovery from their operations; three patients died. One patient (case 9) died at home four and one half months after his discharge from the hospital from carcinoma of the stomach with widespread metastases without having had further massive bleeding, although his stools persistently contained occult blood. Two were hospital deaths; one patient (case 23) died from shock one day postoperatively; the other (case 13), died seven days after an exploratory operation during which a healed duodenal ulcer was found, although the bleeding was observed to come from the stomach. When the stomach was opened no source of bleeding was found. The cause of death was bronchopneumonia. Autopsy disclosed a lymphosarcoma of the stomach that had been overlooked at operation. In one patient in whom the cause of bleeding was not found in 4 operations, multiple complications developed (see case reports). Another, who had a subtotal gastrectomy for a gastric ulcer, apparently bled from a postoperative gastritis nearly two years after his operation. Still another patient, in whom the source of bleeding was not found at exploratory laparotomy after his second hemorrhage, had two more afterward for which no source was discovered clinically.

REPORT OF CASES

CASE 9.—B. S., a man aged 52, was seen on July 12, 1943, four days after he passed a large black shiny stool. The patient continued to work in spite of weakness. The next day he passed several tarry stools, and his family noted that he became pale. The day of admission he fainted in the bathroom. The patient had had a similar but milder episode four years previously, when he was treated at home. After that episode he had an epigastric hernia repaired. Between these two episodes his only complaint was frequent belching and rare heartburn.

On admission the patient was anxious, restless and pale. The temperature by mouth was 99 F., the pulse rate 110 and the blood pressure 110/80. The red blood cell count was 3,320,000 and the hemoglobin 50 per cent. A finger specimen of his stools was positive (4 plus) for occult blood. Otherwise his physical examination revealed normal conditions. He was given one 500 cc. fresh blood transfusion, sedation and nothing by mouth. On his second hospital day he had a large hematemesis followed by shock. He was given two more 500 cc. blood transfusions and treated medically. A gastric analysis showed fasting free hydrochloric acid 18, total acidity 28. After histamine the free hydrochloric acid was 26 and the total acidity 44. His stool became guaiac negative on the tenth hospital day and remained negative afterward. A complete gastrointestinal roentgenologic series on his fourteenth hospital day revealed no demonstrable pathologic condition. A gastroscopic examination was likewise negative. Results of liver function studies were within normal limits. He was discharged on July 30, 1943.

On April 19, 1944 the patient was again admitted to the hospital because of another episode of tarry stools. The hemoglobin level was 64 per cent, the red blood cell count 3,600,000. He was discharged on May 6, 1944 after gastrointestinal roentgenologic series and other tests were negative.

In 1946 he was admitted to another hospital for one more massive upper digestive tract hemorrhage and was discharged within two weeks after further roentgenologic studies were negative. A gastroscopic examination revealed atrophy of his gastric mucosa. Liver function tests were within normal limits.

On Nov. 13, 1947 he was again admitted to the hospital because of another episode of bleeding. For about one month before he passed tarry stools he had had mild epigastric pain that radiated into his back and that came one to two hours after meals but was not relieved by his ingestion of food or alkalies. He had considerable belching. On the day before admission he fainted. He was again studied thoroughly, but no source of his bleeding was discovered. Surgical intervention was advised but was declined by the patient. He was discharged improved on Nov. 26, 1947.

On May 28, 1948 he had another milder episode of bleeding. He was admitted to the hospital but refused to undergo study and exploratory operation and was discharged against advice on June 2, 1948. A repeat gastrointestinal roentgenogram on June 15 revealed a filling defect involving the upper third of the greater curvature of the stomach. The lesion was obviously a carcinoma. The diagnosis was confirmed by a third gastroscopy, and at operation June 22 an inoperable carcinoma of the stomach was found. There were multiple metastases to the regional glands and liver. The patient died at home on Nov. 4, 1948. Autopsy was not performed.

CASE 20.—M. S., a man aged 57, was admitted to the hospital on Oct. 10, 1946 because of a massive gastrointestinal hemorrhage.

He had had two prior hospital admissions, one April 24, 1940 for a ureteral stone, which was passed spontaneously and the other Jan. 9, to 16, 1944 for a comminuted fracture of his left humerus. He also had had an appendectomy in 1943.

The present illness began five to six months before his admission. Several weeks of heartburn and indigestion had subsided spontaneously. Three days before admission he experienced vertigo and weakness; the next day he had diffuse abdominal pain for two hours, and on the day of admission he passed soft tarry stools with a small amount of red blood. This was followed by the vomiting of coffee ground material. He also complained of vertigo and faintness. There was no history of weight loss or anorexia. His bowel movements were regular.

On admission the temperature was 98.6 F., the pulse rate 108, the respiratory rate 15 and the blood pressure 120/78. General physical examination was noncontributory, but the prostate was moderately enlarged and a rectal finger specimen was tarry. The urine was normal. The red blood cell count was 4,960,000, the hemoglobin 90 per cent and the white blood cell count 19,000. The nonprotein nitrogen level was 39 mg., total protein 6.25 Gm. and fasting blood sugar 133 mg., per 100 cc. He continued to bleed despite seven whole blood transfusions given in the next three days, while his red blood

cell count dropped to 2,900,000 and hemoglobin to 3.7 Gm. The blood pressure was transiently maintained.

On the third hospital day he underwent exploratory operation by the abdominal route. The prepyloric region of the stomach and duodenum were opened anteriorly, but no ulcer or bleeding point was found. Then the entire intestinal tract was carefully explored by palpation and visualization, but nothing abnormal was found. A catheter was left in the gastrostomy opening. The patient made an uneventful recovery. The red blood cell count gradually rose to 4,580,000 and the hemoglobin to 11 Gm.

On October 29 a gastrointestinal roentgen examination showed a fixed and slightly dilated loop of ileum a few inches from the ileocecal junction. On November 5 a roentgenogram after the patient received barium enema was suggestive of inflammatory disease of the ileocecal region.

On November 15 he again underwent operation, this time for exploration of the ileocecal region. Minor adhesions were found and easily freed. The distal several inches of ileum were opened and the mucosa carefully inspected. It was normal. The postoperative course of the patient was uneventful.

He was discharged Nov. 28, 1946 with his condition diagnosed as gastrointestinal bleeding, cause unknown.

The patient was readmitted on Nov. 21, 1947 because the night before he had passed tarry stools and fainted. In the morning he vomited coffee ground material. The interval history was essentially noncontributory, except that he had occasional heartburn and much apprehension. He was consistently on a bland diet. On admission the blood pressure was 111/70, the temperature 98 F., the hemoglobin 9.5 Gm. and the stools guaiac positive (3 plus). The nonprotein nitrogen level was 53 mg. and the fasting blood sugar 110 mg., per 100 cc. The clotting time was 2 minutes, the bleeding time 5 minutes. A repeat gastrointestinal roentgenogram on Nov. 22, 1947 showed an irregular duodenal cap. The question was raised whether it was a postoperative defect.

A third operation was performed because the patient continued to lose blood despite repeated transfusions. At operation the stomach and duodenum were negative to palpation. The small and large bowels contained fresh and clotted blood. The stomach was opened along the greater curvature, and the stomach and duodenum found to be normal. The fundus was opened, and fresh bleeding was seen from above. A sigmoidoscope was inserted through this opening and the cardia and lesser curvature well visualized. They appeared normal. Blood was seen oozing from the dome of the fundus, and a small mass was felt on the mucosal side of the fundus. The condition of the patient was poor, and because the lesion was inaccessible the operation was terminated. The patient was discharged on Dec. 19, 1947. On December 30 the patient was readmitted for further surgical treatment of gastrointestinal bleeding. His condition was poor. Melena persisted, and there was an increasing anemia. The hemoglobin on admission was 8.5 Gm. and the red blood cell count 2,650,000. Stools were guaiac positive most of the time.

At this operation the transthoracic approach was chosen. The stomach was opened at the fundus. The fundus and greater curvature of the stomach were widely and completely explored. No source of bleeding was seen.

After this operation there developed empyema and osteomyelitis of the xiphoid bone. The patient was discharged on Jan. 11, 1948.

We last heard from the patient in January 1949, when he complained of pain, nausea and vomiting. The pain was in the epigastrium two hours after meals and was associated with heartburn. There were no further episodes of bleeding while the patient was on a bland diet. Roentgen examination showed a paraesophageal gastric hernia, a deformity of the prepyloric region of the stomach and duodenum; presumably it was due to postoperative scarring.

CASE 23.—J. M., a man aged 43, was admitted to the hospital on Sept. 21, 1947 because of hematemesis. Seven years previously he had had a brief episode of mild epigastric pain, followed in a few days by melena and two episodes of mild hematemesis. He had had another attack of hematemesis two years ago. At that time he was admitted to another hospital, carefully studied and discharged without definite diagnosis of the source of bleeding. He was placed on an ulcer regimen, to which he apparently adhered.

Two weeks before admission he had heartburn unrelated to meals and passed dark stools; later he vomited about 1 pint (500 cc.) of bloody coffee ground material. However, he remained in bed at home. When his condition improved somewhat he entered the hospital for further study. On his admission a finger specimen of his stool was positive (2 plus) for occult blood. The temperature was 98.6 F., the pulse rate 90 and the blood pressure 160/90. The hemoglobin level was 35 per cent, the red blood cell count 2,130,000 and the white blood cell count 9,800. The urine was normal. The icterus index was 4 and the nonprotein nitrogen level 50 mg. per 100 cc. His stools remained positive for occult blood for four days, then became negative. He received two whole blood transfusions. A gastrointestinal roentgen examination revealed nothing abnormal. The gastric analysis revealed normal secretions. Gastroscopic examination was refused. Results of serial liver function tests were within normal limits. He was discharged improved on Oct. 4, 1947.

On May 30, 1949 he had another episode of tarry stools. He was readmitted to the hospital and treated medically. His red blood cell count was 2,800,000, hemoglobin 40 per cent. One transfusion of whole blood was given. Gastrointestinal roentgen examination and that of the gallbladder after the patient received tetraiodophthalein sodium (Graham test) revealed essentially normal conditions. He was discharged June 14, 1949. Another roentgenogram in July 1949 revealed a deformity of the duodenum, and a diagnosis of duodenal ulcer was made.

In October 1949 the patient again vomited blood for one day. This episode was followed by tarry stools for six days. His hemoglobin at its lowest reading was 55 per cent and his red blood cell count 2,650,000. Subsequently he had persistent epigastric pain which at times became excrutiating. It was not related to meals and radiated into his back. This persisted despite a regimen of complete bed rest, ulcer diet, alkalies and belladonna.

On Dec. 1, 1949 he again passed black stools. The same day he vomited a pint of bloody and coffee ground material. A week later another gastrointestinal roentgen examination revealed flattening of the lesser curvature of the media of the stomach by extrinsic pressure and questionable evidence of a healed duodenal ulcer. The gallbladder showed poor filling and good concentration of the dye. Because of his weakness and persistent pain the patient was again admitted to the hospital on December 15, at which time jaundice was noted; the liver was palpable 3 fingerbreadths below the costal margin and was irregular. The hemoglobin was 7.5 Gm., the hematocrit 27, the white blood cell count 9,800. The urine showed a trace of albumin, bile (2 plus) and no urobilinogen. The blood pressure was 200/104. The nonprotein nitrogen level was 13 mg., per 100 cc., the carbon dioxide-combining power 43 volumes per cent, the icteric index 35, the cephalin-cholesterol flocculation zero, thymol turbidity 4.9 units and serum bilirubin 2.9 units, later 4.13 units. While the patient was under observation his liver was observed to enlarge and become irregular. There was no response to repeated blood transfusions.

On Dec. 30, 1949 he underwent operative intervention. The liver was studded with nodules. A biopsy specimen was taken. The patient died the next day in shock. Autopsy was refused. The microscopic diagnosis was adenocarcinoma probably originating in the bile ducts.

COMMENT

A definitive diagnosis of the cause of bleeding is often impossible in massive, exsanguinating or even rapidly fatal cases of upper digestive tract hemorrhage. Hence, many patients are discharged from the hospital without localization of the source of trouble. Obviously a still greater number present a diagnostic problem on admission. Early roentgen examinations whenever possible and early clinical studies, including esophagoscopy and gastroscopy when indicated, reduce the number of

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cases in which origin of the bleeding remains undetermined. However, in studying these patients one should bear in mind the definite limitations in the roentgenologic diagnostic technic as described by Hampton,[7] Schatzki [8] and others. If a lesion is not located soon after admission of the patient a repeat examination is indicated before he is discharged. To a lesser degree this also applies to gastroscopy.

The difficulty in the determination of the etiological basis of such bleeding in some cases is well known and is emphasized by frequent failures in this respect even with careful surgical exploration and the occasional inability to demonstrate the source of bleeding at autopsy.[9]

Patients who had one hemorrhage of undetermined origin, massive or otherwise, should be carefully observed afterward. They should be intensively studied at intervals in the hope of establishing a definitive diagnosis. In our own experience, an ultimate clinical diagnosis of the source of the hemorrhages was made in nine patients, or 33 per cent. The diagnosis was confirmed by surgical intervention in five cases. In one patient it was based on roentgenologic evidence alone, in two instances on gastroscopy and in one on clinical and laboratory observations.

Surgical exploration was advised in patients with repeated episodes of massive unexplained upper digestive tract hemorrhages. Such exploratory laparotomies were performed in five patients, in four after repeated hemorrhages and in one during his first but persistent episode of bleeding despite multiple transfusions. In only two patients, or 40 per cent, was the source of bleeding found at operation (cases 3 and 17). Thus an ultimate diagnosis as to the source of bleeding was made in 11 cases, or about 40 per cent.

The high percentage of patients who declined to undergo surgical exploration must be mentioned. The reasons for these refusals can be found in the frank explanation that the recommended operations are exploratory in character, that the cause may not be found and that further hemorrhages may occur. This together with the absence of or only minimal digestive symptoms between the bleeding episodes most likely accounts for 50 per cent refusal in this group. In retrospect, in the light of our experience, one wonders whether these patients did or did not act wisely.

Three patients died. All underwent operation and all had malignant disease. One patient died four and one half months postoperatively of an inoperable carcinoma of the stomach. However, this lesion does not explain his hemorrhages, which to our knowledge had begun five years before his death. One may postulate a previously overlooked ulcer or an adenomatous polyp in the cardiac end of the stomach, which finally became malignant. Another patient, who died of shock after an exploratory laparotomy, had a primary carcinoma of the extrahepatic bile ducts with widespread metastases. In this instance also it is difficult to explain his many hemorrhages, dating back to 1942. The third patient had an exploratory operation but no source of bleeding was found. She died of bronchopneumonia. Autopsy disclosed a lymphosarcoma not recognized during the operation.

The immediate medical or combined medical and surgical treatment of massive upper digestive tract hemorrhages is not discussed here and will be presented in a future contribution. Because of the limited number of patients in this series, valid statistical studies cannot be made. However, several interesting and probably significant observations will bear emphasis. A relatively large number of patients in this group were females. The age distribution is about the same as that in peptic ulcer. Surgical exploration does not seem to be superior to prolonged and careful clinical observation in the determination of the source of the bleeding, and it carries a greater risk in the debilitated patient. However, surgical intervention may disclose some lesion which otherwise could not be discovered. If the patient who is receiving medical treatment does not die from his first massive hemorrhage the mortality rate seems to be low with consequent hemorrhages. In this respect the hemorrhages from undetermined origin are similar to those from proved ulcers.[10] In rare cases, in which the bleeding persists despite adequate and proper treatment, one may be forced to explore the abdomen surgically. However, even in such cases, in which the stomach and/or the bowels may be filled with blood, a demonstrable cause for the bleeding may not be found.

If and when the origin of an upper digestive tract hemorrhage is definitely diagnosed, further management must depend primarily on the diagnosis.

SUMMARY AND CONCLUSIONS

A follow-up study is reported of 27 patients who have been observed during and after one to five massive digestive tract hemorrhages of undetermined origin. The patients were intensively studied both during and after the bleeding episodes. A clinical diagnosis of the source of the hemorrhage was eventually made in 9 patients. The origin of the bleeding was found on surgical exploration in 2 cases. The cause of the hemorrhages was not discovered in 16 patients, in three despite a total of six exploratory laparotomies.

Intensive and prolonged clinical observation of patients with one or more massive upper digestive tract hemorrhages of undetermined origin eventually permits a definitive diagnosis of the cause of the bleeding in nearly as many cases as would exploratory operations. However, in a few instances such surgical explorations are the only means of arriving at a definitive diagnosis.

Medical management of patients is advised during and after a single massive upper digestive tract hemorrhage of undetermined origin. Surgical exploration is recommended after the patient has had repeated hemorrhages.

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ROLE OF TRANSFUSIONS IN THE MANAGEMENT OF GASTRIC HEMORRHAGE

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When a sudden, large hemorrhage occurs from peptic ulcer, there is usually a fall in blood pressure as a result of an abrupt reduction in the circulating blood volume. This initial fall in blood pressure, if not too great, may be of benefit in preventing further hemorrhage. Blood clots more rapidly after a severe hemorrhage, and this plus the low blood pressure is usually effective in sealing the leak even in large vessels. In the case of arteries, retraction of the middle fibromuscular coat and curling of the endothelial lining are further defenses against bleeding.[1] If these natural mechanisms fail for some reason (for example, arteriosclerosis or erosion of a main artery) there will be continuing hemorrhage or recurrent hemorrhage with persistent shock; such patients face the dangers of anoxemia of vital organs resulting in death.

The role of blood transfusion therapy in hemorrhage from peptic ulcer consists first in the cautious withholding of transfusions at the onset of hemorrhage. This permits the physiological mechanisms to bring about cessation of hemorrhage in a majority of cases. At any stage, transfusions must be employed in sufficient quantities to avoid anoxemia.

WITHHOLDING TRANSFUSIONS

Opposition to the liberal use of blood transfusions during peptic ulcer hemorrhage has been based on the idea that they may increase the blood pressure to a point high enough to prevent clot formation or to dislodge clots already formed.[2] The chief evidence against the liberal use of transfusions consists of (1) reports showing an increased incidence of recurrent bleeding and higher mortality in patients receiving immediate transfusion as compared with delayed transfusion [3] and (2) reports showing an increased mortality rate from bleeding ulcer during the period since the introduction of transfusion therapy, as compared with the era before the use of blood transfusions.[4] Most of these reports, however, represent a period when transfusions were given rapidly and reactions were frequent. More recently, Jones [5] has listed the risks of blood transfusion as reactions, jaundice, Rh antibody difficulties and overloading the circulation. With the introduction of slow drip transfusions and improved methods of blood typing, the increased safety of blood transfusion has led to more frequent use of transfusion therapy in general. Studies of blood pressure changes during slow drip transfusion have not demonstrated any sudden change in blood pressure unless the patient was in shock.[6]

During the six year period, 1943-1949 there were 108 patients with peptic ulcer admitted to the University Hospital with active bleeding (table 1). The use of transfusions during active hemorrhage in these cases has been correlated with continued or recurrent bleeding and death (table 2). Inasmuch as transfusions are usually reserved for the more serious cases—in which the mortality rate and incidence of continued hemorrhage can be expected to be greatest—these cases have been divided for more accurate analysis according to the severity of hemorrhage. Mild to moderate hemorrhage denotes those ears in which the hemoglobin remains above 7.8 Gm., the red blood cell count above 2,500,000 per cubic millimeter and the hematocrit above 30 per cent. Severe hemorrhage includes those cases in which the blood values fall below these figures, the patient exhibits pronounced or recurring shock, the patient rapidly exsanguinates before hemodilution and resultant anemia can occur or the hemoglobin continues to decrease after 1,000 cc. of blood has been given to the patient during a 24 hour period.

TABLE 1.—*Diagnosis, Severity of Hemorrhage and Mortality in 108 Cases of Bleeding Ulcer*

Type of Ulcer	Total Cases	Severe Hemorrhage	Death
"Peptic"	11	5 (45.5%)	2 (18.1%)
Duodenal	70	30 (42.9%)	9 (12.8%)
Gastric	17	6 (35.3%)	2 (11.7%)
Jejunal	9	8 (88.9%)	1 (11.1%)
Gastric and duodenal	1	1	0
Total	108	50 (46.3%)	14 (12.9%)

TABLE 2.—*Transfusion During Hemorrhage Correlated with Further Hemorrhage*

	No Further Hemorrhage	Further Hemorrhage		
		Continuous	Recurrent	Death
Mild to moderate hemorrhage				
No transfusion (47 cases)	87.2%	8.5%	4.2%	0
Transfusion (11 cases)	72.7%	27.2%	0	0
Severe hemorrhage				
No transfusion (12 cases)	50.0%	33.3%	16.6%	16.6%
Transfusion (38 cases)	34.2%	44.7%	21.0%	31.5%
Total group				
No transfusion (59 cases)	79.6%	13.5%	6.7%	3.3%
Transfusion (49 cases)	42.8%	40.8%	16.3%	24.5%

The incidence of further hemorrhage as well as the mortality is higher in all groups of patients receiving transfusions during active bleeding. This correlation is undoubtedly due in part to the preferential use of transfusions in cases in which bleeding is prolonged because of pathological conditions—for example, ero-

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6. Jones, F. A.: Hematemesis and Melena, Observations on the Use of Continuous Drip Transfusions, Brit. M. J. **1**: 689, 1943. Gray, S. J.: The Management of Patients with Massive Hemorrhage from Peptic Ulcer, M. Clin. North America **31**: 1121, 1947.

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sion into a main artery, arteriosclerosis or the fixation of a vessel in the firm scar tissue of chronic ulceration, resulting in inability of the vessel to contract or constrict the lumen. Another possible factor is the promotion of continued or recurrent hemorrhage as a result of too rapid increase in blood volume with blood transfusions.

Because the drop in blood volume at the beginning of a hemorrhage favors cessation of bleeding and clot formation, this natural mechanism should not be unduly disturbed by the rapid introduction into the circulation of large amounts of fluid during the first few hours after the onset of hemorrhage, provided severe shock does not occur. Beyond this period, this advantage is offset by the spontaneous increase in circulating blood volume which results from withdrawal of fluid from the tissues into the blood stream.

INDICATIONS FOR TRANSFUSION

Specific indications for transfusion include (1) a systolic blood pressure below 90 mm., with rising pulse rate or other clinical manifestations of shock and (2) a fall in hemoglobin to 50 per cent or below. The amount of blood to be given must of necessity be determined by the severity of shock, the rapidity of hemorrhage and the degree of anemia. In most circumstances the infusion of 500 cc. of citrated blood by slow drip over a three to four hour period, repeated as often as necessary to control shock and anemia, will suffice. In persistent hemorrhage the amount of transfused blood required to maintain a stable hemoglobin level will be an index of the rate of bleeding.

The chief roles of blood transfusion include (1) prevention of death from exsanguination; (2) alleviation of hemorrhagic shock; (3) prevention of damage to vital organs by anoxemia; (4) maintenance of the hemoglobin at a sufficiently safe level so that a recurrent hemorrhage will not threaten life, and (5) preservation of the patient in suitable condition for possible surgical intervention.

The loss of over 30 per cent of the total blood volume from brisk hemorrhage will usually cause death unless transfusions are given. Blood volume determinations represent the most accurate index of the severity of a hemorrhage, but such studies are not generally available. The hemoglobin, red blood cell count and hematocrit determinations are valuable, but they tend to lag behind the clinical course of the patient; therefore the best immediate guides to transfusion therapy in a continuing hemorrhage are the clinical observations—falling blood pressure, rapid pulse rate and other manifestations of shock.

When hemorrhagic shock occurs, blood must be given in sufficient amount to avoid the dangers of anoxemia. If the blood pressure falls below a certain critical level, impaired blood supply to the vasoconstrictor center causes it to become weakened and lose its tone; this results in further decline of blood pressure.[7] Cerebral anoxemia is indicated by mental confusion of any degree, for example, impaired memory for recent events. Prolonged shock will cause prerenal azotemia with lowered urinary excretion and elevated blood urea nitrogen levels. Wood [8] has suggested that a fresh erosion of devitalized tissue around an ulcer may cause recurrent hemorrhage.

The hemoglobin must not be permitted to drop to a level where a recurrent hemorrhage will threaten life. The minimum level of safety is usually placed at 40 to 50 per cent [9] (6.2 to 7.8 Gm.). There have, of course, been many patients who have survived additional hemorrhage in the presence of greater degrees of anemia. Although it is not possible to predict which patients will cease bleeding on conservative management and which will require operation to control hemorrhage, statistical studies of bleeding ulcer cases in the past have indicated increased mortality rates in certain patients. These prognostic factors may be utilized to indicate the patients who are potential surgical candidates and who require adequate blood replacement to maintain them in optimum condition for operation. These factors have been evaluated in the 108 cases studied at the University Hospital.

TABLE 3.—*Evaluation of Prognostic Factors in Peptic Ulcer Hemorrhage*

Factor	Cases	Severe Hemorrhage, %	Death, %
Sex: Male	95	46.0	13.5
Female	13	46.0	7.6
Age: Under 45	33	51.5	12.1
Over 45	75	44.0	13.3
Number of previous hemorrhages			
0	48	47.9	22.9
1	34	50.0	2.9
2	10	30.0	10.0
3	8	37.5	0
More than 3	8	50.0	12.5
Significance of hematemesis			
Hematemesis with or without melena	81	48.1	14.8
Melena alone	27	40.7	7.4
Significance of recurrent hemorrhage			
Recurrent hemorrhage	12	83.3	16.6
Hemorrhage continuous over 24 hr.	31	77.4	38.7
Hemorrhage on full ulcer regimen	4	100.0	75.0
Duration of previous ulcer symptoms			
None	5	80.0	80.0
Under 4 wks.	7	71.4	14.2
Over 4 wks.	96	42.7	9.3

PROGNOSTIC FACTORS

Type of Ulcer.—In the experience of Welch,[10] bleeding gastric ulcer, because of frequent erosion of the right or left gastric artery, carries a higher mortality than duodenal ulcer. In the present series the mortality rate has been approximately the same for gastric, duodenal or jejunal ulcer (table 1). The highest mortality occurred in patients having gastroduodenal hemorrhage with symptoms suggestive of ulcer, but in whom roentgen evidence of ulcer was lacking.

Sex.—Bleeding from peptic ulcer is seen more frequently in men than in women, and the mortality rate is usually considered to be higher in men than in women. In the present series, the mortality in men was almost twice that in women (table 3).

7. Amendola, F. H.: The Management of Massive Gastroduodenal Hemorrhage, Ann. Surg. **129**: 47, 1949.

8. Wood, I. J.: The Bleeding Peptic Ulcer, M. J. Australia **2**: 1031, 1937.

9. Jones, F. A.: Haematemesis and Melena, Brit. M. J. **2**: 441, 1947. Bennett, T. I.; Dow, J., and Wright, S.: Severe Haemorrhage from Stomach and Duodenum, II. General Lines of Treatment, Lancet **1**: 551, 1942.

10. Welch, C. E.: Treatment of Acute, Massive Gastroduodenal Hemorrhage, J. A. M. A. **141**: 1113 (Dec. 17) 1949.

Age.—The majority of ulcer hemorrhage deaths occur in patients over 45 years of age.[11] This is probably a reflection of the higher incidence of arteriosclerosis and other complicating diseases in the older age group. In the present series, however, the mortality in the age group under 45, in which bleeding was less frequently seen, was only slightly less than in the older age groups, emphasizing that youth in itself does not immunize against a fatal termination (table 3) and that older patients do not necessarily face a higher mortality because of their age.

Number of Previous Hemorrhages.—Most deaths from bleeding peptic ulcer occur during a first hemorrhage.[11] In the present series, 22.9 per cent of those ulcer patients bleeding for the first time died; in patients undergoing a second or third hemorrhage, the mortality rate was considerably less (table 3).

Significance of Hematemesis.—Cases associated with hematemesis carry a graver prognosis than when melena alone occurs, possibly because hematemesis is a reflection of more copious hemorrhage. In this series the presence of hematemesis produced a mortality rate twice that of melena alone (table 3).

Significance of Recurrent Hemorrhage.—Patients who cease bleeding soon after admission to the hospital, and who have a recurrent massive hemorrhage a day or so later, show a sharp increase in mortality.[12] In this series 12 patients had recurrent hemorrhage and seven (16.6 per cent) died. The presence of continuous hemorrhage for more than 24 hours after admission was of more significance; there were 31 such cases with a mortality of 38.7 per cent.

TABLE 4.—*Fatal Cases*

Age	Ulcer	Complication	Operated on During Hemorrhage
56	Gastric	Postop. cystotomy	
82	Duodenal		
27	Acute gastric	Tuberculous meningitis	
71	Duodenal	Arteriosclerotic heart disease	x
61	Duodenal		
44	Peptic	Perforation	
55	Duodenal	Postop. cholecystectomy	
42	Duodenal	Hypertension	
64	Jejunal		x
75	Duodenal	Terminal nephritis, uremia	
62	Duodenal	Postop. resection for cancer of colon	
63	Peptic		
64	Duodenal		
Newborn	Duodenal	Perforation; multiple congenital abnormalities; pneumonia	x

Patients Bleeding Despite Full Ulcer Regimen.—Four patients bled while hospitalized and following a full medical ulcer regimen, and three died. The poor prognosis in such cases was pointed out previously by Holman.[13]

Duration of Ulcer Symptoms.—Christiansen [14] stated that the absence of previous ulcer symptoms indicates a better prognosis in ulcer hemorrhage than does such a history. In the present series, however, the patients without previous ulcer symptoms had a higher mortality rate than those with symptoms of more than one month.

Elevated Blood Urea Nitrogen.—A persistently elevated or rising blood urea nitrogen level sometimes indicates a poor prognosis, usually being an index of continued bleeding or shock.

Severity of Hemorrhage.—Severe hemorrhage is always accompanied with higher mortality rates. The severity of hemorrhage will be determined not only by the amount of blood loss but also by the rate of bleeding. When hemorrhage is classified by the method mentioned earlier, severe hemorrhage occurred in 50 patients, of whom 13 (26 per cent) died.

Presence of Complicating Disease.—One of the most important factors causing the high mortality rate in this series was complicating disease, as shown in the summary of fatal cases (table 4). This is a reflection of the type of case seen in this hospital, to which the majority of patients with bleeding ulcers are referred for admission because of failure to stop bleeding by use of conservative measures elsewhere or because of complicating disease. In the entire series, pyloric obstruction of some degree was present in 13 cases, with no deaths. The combination of perforation and hemorrhage occurred in two patients, both of whom died.

On the basis of the literature as well as observations in the cases in this series, it would appear that the most unfavorable prognostic factors include: (1) patients over age 45, but youth is no immunity against exsanguination; (2) patients experiencing a first hemorrhage; (3) hematemesis; (4) hemorrhage persisting over 24 hours after admission to the hospital, or recurrent hemorrhage; (5) patients bleeding while already following a full medical ulcer regimen, and (6) coexisting complicating disease. Such patients warrant especially careful observation as potential surgical candidates; they should receive blood transfusion in sufficient amount to keep them good surgical risks.

SUMMARY

1. Cautious withholding of blood transfusions during the first few hours after the onset of hemorrhage from bleeding peptic ulcer (unless shock occurs) may favor clot formation and cessation of bleeding.

2. Transfusions are indicated for control of shock and for prevention of harmful effects of anoxemia on vital organs. The hemoglobin must be maintained above a level at which continuing or recurrent hemorrhage will not threaten life; the suggested level is 50 per cent.

3. Prognostic factors which in the past have been associated with high mortality rates may be utilized to indicate potential surgical candidates. Liberal transfusion therapy is particularly indicated for such patients in order to keep them good operative risks.

ABSTRACT OF DISCUSSION

ON PAPERS BY DRS. POLLARD AND WOLLUM, JANKELSON AND MILNER, AND LIPP AND OTHERS

DR. DWIGHT L. WILBUR, San Francisco: This symposium on bleeding from the upper gastrointestinal tract shows clearly the wide divergence of experience of observers in the incidence of bleeding, the frequency of various causative factors and the advantages and disadvantages of various methods of treatment, particularly transfusion. Drs. Jankelson and Milner indicate the advantages of the follow-up of patients as a diagnostic procedure. Although their current series is too small to lead to significant conclusions, it suggests that in well over half of the cases a prolonged period of observation did not lead to an explanation for the bleeding if it was not at first apparent. Use of transfusions for the treatment of patients with bleeding peptic ulcer probably is the greatest advance in recent years in the management of such patients. The establishment of blood banks has greatly simplified and enlarged this aspect of treatment. I agree with Drs. Pollard and Wollum that immediate transfusion should be withheld except for patients in shock and that it is wise to give blood slowly. Dr. Lipp and his colleagues struck a keynote in the management of patients with gastrointestinal bleeding when

11. Blackford, J. M., and Williams, R. H.: Fatal Hemorrhage from Peptic Ulcer, J. A. M. A. **115**: 1774 (Nov. 23) 1940.
12. Baker, C.: Bleeding Peptic Ulcer, Guy's Hosp. Rep. **96**: 1, 1947.
13. Holman, C. W.: Further Observations on the Treatment of Bleeding Peptic Ulcer, Surgery **23**: 405, 1948.
14. Christiansen, T.: On Massive Hemorrhage in Peptic Ulcer, Acta med. Scandinav. **84**: 374, 1935.

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they stated that "generalization and conclusions drawn from series of patients are grossly inadequate when one is confronted with a patient with massive hemorrhage. The individual patient remains an individual problem." Their suggestion of a "transfusion test" is most interesting, and one which is tried in a small way by most physicians who treat such patients. It would seem unwise except in cases of the severest bleeding to advocate use of 2,000 cc. of blood in one hour or 5,000 cc. in six hours. There are economic and practical factors which may be added to the unwisdom of such procedures. If a transfusion test is done on the lesser scale, however, it may be an excellent indication of the need for surgical treatment. As an internist I am stimulated by these papers to conclude that surgical treatment of bleeding has great advantages under three conditions; first, when it is obvious that bleeding cannot be controlled by medical means; second, when the lesion present is of long duration or is in the stomach and of questionable nature, and finally, when there have been repeated (three or more) hemorrhages without apparent clinical cause. Although surgical exploration may not always reveal the cause of the bleeding in patients of the last group, it commonly will do so and will permit correction of the lesion sufficiently often to warrant more frequent use of this method of treatment.

DR. KENNETH C. SAWYER, Denver: These papers have been exceptionally stimulating and reassuring because each emphasizes treatment of individual patients instead of attempting to establish criteria for treating groups of patients with massive upper digestive tract bleeding. In reviewing the literature one is impressed with the universally good results obtained by the methods of treatment advocated by the person reporting his particular series of cases. Nevertheless, when the individual physician encounters a massive upper gastrointestinal tract hemorrhage the problem of treatment immediately becomes grave. The surgeon becomes "medically minded," and even the most conservative internist begins thinking of a qualified surgeon. If the case is managed properly the internist and surgeon will spend 24 hours a day either with or near the patient. Teamwork is essential. I stress individualization because during a 12 month period it was my misfortune to see three patients (an 8 week old baby, a 22 year old soldier and a 32 year old mother) die from an untreated or conservatively treated hemorrhage from duodenal ulceration. Later, while I was performing a total resection of the stomach for the treatment of carcinoma the inferior vena cava was inadvertently torn. During an 11 minute interval our anesthesiologist, Dr. J. Lawrence Campbell, infused the patient with 1,500 cc. of whole blood. The laceration in the vena cava was sutured, and the patient was restored to his farm and family. This experience reemphasized the value of teamwork in major surgical procedures and demonstrated the feasibility of operating on a patient with a peptic ulcer during the phase of active bleeding. This principle has been applied to massive upper gastrointestinal tract hemorrhage in nine instances within a two year period without mortality. Three patients of Drs. Jankelson and Milner exhibited intestines full of blood, and careful exploration of the gastrointestinal tract failed to reveal the source of bleeding. In each instance a high gastric resection was performed. Examination of the interior of the stomach revealed an ulceration with an open vessel high on the lesser curvature in the three resected specimens. We agree that (1) upper gastrointestinal tract bleeding is usually a case for medical treatment; (2) a preoperative diagnosis is desirable but occasionally impossible because the patient's condition does not warrant the delay necessary to make an anatomic diagnosis, and (3) if blood is escaping from a patient faster than it can be replaced, definitive and immediate surgical treatment is indicated. The value of high gastric resection when the bleeding point cannot be found has been proved in a limited series of cases.

DR. RUDOLF SCHINDLER, Los Angeles: Gross hemorrhage may occur in each of the three chief types of chronic gastritis. In 200 subsequent cases of chronic gastritis gross hemorrhage was noticed 22 times, namely, in seven cases of chronic hypertrophic gastritis (usually from small ulcerations, and such a hemorrhage may lead to death); in seven cases of superficial gastritis (also from superficial erosions), and in eight cases of chronic atrophic gastritis (a form in which the hemorrhage is usually parenchymatous). Furthermore, sometimes one sees noninflammatory hemorrhagic erosions bleeding profusely. However, there are some obscure gross gastric hemorrhages without varices, without ulcer and without tumor, in which at gastroscopy gastritis is not found, as shown earlier by Dr. Jankelson. Former experiments of mine on the hypnotic production of skin hemorrhages have become rather well known through Dunbar's book. Two women were observed who suffered for years from extensive skin hemorrhages and in whom the most careful physical and laboratory examinations did not reveal any disease. It finally became apparent that these women had major hysterical psychoneurosis. It was possible to produce these skin hemorrhages by hypnotic suggestion at any predetermined place. Plaster casts were used to avoid artefacts. Finally blisters with sanguineous content developed. It is known how much I object to the uncritical generalization of psychosomatic relationships. The observations mentioned leave little doubt, however, that psychogenic hemorrhages do occur. In a case of unexplained gross gastric hemorrhage one has the right to consider this possibility if all objective methods, including gastroscopy, are negative.

DR. WALTER L. PALMER, Chicago: I hope Dr. Sawyer will publish the case he mentioned of the 8 week old baby dying of massive hemorrhage. Deaths from bleeding in infants are generally attributed to vitamin K deficiency, although the older literature contains many reports of peptic ulcer with massive hemorrhage in the early weeks of infancy. When John B. Murphy in 1892 first described the operation for acute appendicitis he wrote that the progress of the disease had to be watched with knife in hand. Massive hemorrhage, as these gentlemen have all brought out, also must be watched with knife in hand, although the number of patients who have to undergo operation is small. In Dr. Lipp's presentation there was implicit the fact that the patients were watched hour by hour and not day by day or week by week. Dr. Sawyer brought out the same point. These patients are in a state of critical emergency and things may go wrong very rapidly. Blood in large amounts must be available to be given immediately, and if the hemorrhage does not cease within a few hours, as evidenced by Dr. Lipp's transfusion test, then operation is certainly indicated. In the *Archives of Internal Medicine* (**27**:102 [Jan.] 1921 and **48**:836 [Nov.] 1931) I reported cases of heredofamilial angiomastosis with recurring hemorrhages (Rendu-Osler-Weber's disease), including instances of gastric and intestinal bleeding of telangiectatic origin without evidence of ulcer. In July 1946 in San Francisco I discussed before this section "Unusual (Benign) Hematemesis: Gastric Telangiectatic Dysplasia" (*Rev. Gastroenterol.* **14**:258, 1947). I cited some cases with a view of the literature. Among other investigators, Kessel (*J. A. M. A.* **97**:1058 [Oct. 10] 1931), Kushlan (*Gastroenterololgy* **7**:199, 1946), Rundles (*Am. J. M. Sc.* **210**:76, 1945), Renshaw (*Cleveland Clin. Quart.* **6**:226, 1939), Macklin (*Scient. Monthly* **52**:56, 1941), McDonough, Dry and Roth (*Proc. Staff Meet., Mayo Clin.* **15**:593, 1940), Voyles and Ritchy (*Ann. Int. Med.* **22**:730, 1945) and Boston (*Am. J. M. Sc.* **180**:798, 1930) have reported such cases of severe massive hemorrhage from the stomach without positive evidence of ulcer but caused by bleeding telangiectases. Gastric resection has been done unnecessarily in some of these cases. (Leo Kessel, B. B. Crohn and Asher Winkelstein of New York know of such cases.) I have encountered several such cases during the past 40 years and have seen several more with other physicians. A. H. Aaron of Buffalo had one such patient and E. B. Benedict of Boston (*Am. J. Roentgenol.* **47**:254, 1942) cites one such case. The use of rutin, snake venom injections, topical thrombin (by means of the Miller-Abbott tube) oxidized cellulose (oxycel®), absorbable gelatin sponge (gelfoam®) and blood transfusions often obviates the need of radical surgical

procedures in this type of massive gastric hemorrhage. Although this condition is not at all common, it should be kept in mind. Of course, such a patient may also have an ulcer or a malignant lesion. I would like to ask Drs. Jankelson, Pollard, Lipp and associates of their experience with such cases. I believe that Dr. Pollard performed gastroscopic examination of Rundles' patient. Finally, in case 14 Seligmann (*J. Mt. Sinai Hosp.* **5**:165, 1938) reported that a man aged 73 (on George Baehr's service) had a bleeding duodenal ulcer and hereditary hemorrhagic telangiectasia.

DR. I. R. JANKELSON, Boston: There is no doubt that gastritis can be a real cause of massive hemorrhage. In recent years our technic in management of these cases has changed, in that roentgen examination is done almost on admission of the patient to the hospital except in cases of profound shock. Early gastroscopy, especially in those cases in which no lesion or only suspicious lesions are found by roentgenologic studies, many more cases of gastritis could be demonstrated than in the old routine when it was performed 10 to 14 or more days afterward. As far as a psychogenic cause of hemorrhage is concerned, I know nothing about it and was interested to hear Dr. Schindler's comments. The late morbidity of hemorrhage can be divided into two groups. One is persistent anemia. In some cases we have observed severe and persistent anemia which apparently remained stable at a certain blood level. It is difficult to overcome except by repeated blood transfusions. The other group is dependent on the cause of the hemorrhage. If the patient has an ulcer which has bled profusely or repeatedly, one still has the problem of treating the ulcer. The same applies to cirrhosis of the liver or whatever may be the cause of hemorrhage.

DR. RUSSELL S. BOLES, Philadelphia: Dr. Lipp mentioned a death following radiological examination of one of his patients who was suffering from hemorrhage. This is a matter of great importance, and there is quite a difference of opinion on the best time to examine radiologically these patients with hemorrhage in order to determine whether they actually have an ulcer. I think this audience, Dr. Lipp, might be interested in hearing your comments on this subject.

DR. H. MARVIN POLLARD, Ann Arbor, Mich.: Analysis of our statistical data would lead one to believe that the results in those that had the late transfusion, even with a severe hemorrhage, were, so far as mortality figures are concerned, slightly better than in those who received early transfusions. As soon as the evidence of shock becomes profound, the blood pressure starts falling, the pulse rate starts rising and the hemoglobin goes down on each successive count, even though you are following the patient at hourly intervals, the patient should receive transfusions. However, those patients with a moderate hemorrhage are better off to have delayed transfusions, as Dr. Wilbur suggested, after several days when the hemorrhage has stopped completely.

DR. WILLIAM F. LIPP, Buffalo: In answer to the question of Dr. Boles, the patient in the first 6 year period who died immediately after radiographic examination died with a single, sudden, massive expulsion of blood, and this was apparently his first and only hemorrhage. Although it is probable that there was a relationship between the roentgenologic study and the bleeding, it may have been coincidental. We believe that it is seldom necessary to make roentgen examinations in patients who have just experienced massive hemorrhage, for it is unlikely that the results will change the type of therapy. However, such studies are indicated occasionally, and I think they can be done with relative safety provided there is no manipulation. The results of such examinations are not always satisfactory in demonstrating the source of the bleeding. Our discussion this morning was limited solely to the problem of acute massive hemorrhage; we did not discuss the elective use of definitive surgical procedures following one or more gastric hemorrhages.

1. Barnett, M. R.: The Impact of Blindness, read at Mobilization to Prevent Blindness, New York City, May 24, 1950.

2. Berens, C.; Kerby, C. E., and McKay, E. C.: The Causes of Blindness in Children, J. A. M. A. **105**: 1949 (Dec. 14) 1935.

THE BATTLE AGAINST BLINDNESS

Walter B. Lancaster, M.D., Boston
and
Franklin M. Foote, M.D., New York

If one can visualize a city larger than San Diego, California or Akron, Ohio—a city the size of Miami, Fla., Omaha, or Providence, R. I.—in which every man, woman and child is blind, one begins to grasp the extent of our estimated blind population of 260,000 and what it means to the person and his family. Basing our figures on sample statistical studies and the age distribution of the population, we estimate that each year 22,000 additional persons have their visual acuity reduced to 20/200 or less. Blindness is a major public health problem not merely because of its incidence but also because the blind man or woman does not die soon, as does the victim of cancer, but lives on for many years, often partly or wholly dependent on others. This fact makes blindness of great economic as well as humanitarian significance. For the inadequate care and services to the blind that we are now giving we spent last year over $125,000,000 in tax and private funds.[1] In striking contrast to these sums we had last year somewhat less than $1,000,000 available for research in the blinding eye diseases and less than $500,000 for organized prevention services. We should not reduce activities for those already blind, but by increasing what we are doing now to enable persons to keep their sight we can gradually reduce the number of the unnecessarily blind.

TABLE 1.—*Causes of Blindness by Etiological Factors**

Etiological Factors	Percentage of Total, All Ages (Est.)
Infectious diseases	22.5
Trauma	9.3
Poisonings	0.6
Neoplasms	0.9
General diseases	5.5
Prenatal origin	12.2
Unknown to science	29.9
Undetermined or not specified	19.1

* Observations in this table and in table 2 are based on data covering 3,905 children in schools and classes for the blind (Kerby [2]) and 46,537 adults receiving aid to blind (from reports compiled by state public assistance agencies, including those covered in study published in 1947 by the Social Security Administration [3]).

CAUSES OF BLINDNESS

For many years the statistical division of the National Society for the Prevention of Blindness has studied the causes of blindness in those states where ophthalmologic diagnoses are available for recipients of aid to the blind or for blind children. By use of the standard classification [2] these causes have been tabulated and analyzed.

From table 1 it is apparent that over one fifth of the blindness in the United States is caused by infection.

From the National Society for the Prevention of Blindness, 1790 Broadway, New York 19 (Dr. Foote).

Read before the Section on Ophthalmology at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 30, 1950.

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Since the founding of the National Society in 1908 by Park Lewis and Louisa Lee Schuyler there has been a remarkable decrease in blindness due to infection. Because of legislation, educational activities and better medical treatment, there has been a decline in blindness from ophthalmia neonatorum among new admissions to schools for the blind from 28 per cent in 1908 to 2.2 per cent in 1948. Case finding through widespread serologic tests for syphilis, particularly premarital and antepartum blood tests, together with improved treatment, probably is responsible for the 50 per cent decrease in syphilis as a cause of blindness among children in schools for the blind since 1936.

About one tenth of blindness is due to injury. The actual figure undoubtedly is higher than this, because blind persons receiving workmen's compensation are not reported. Ten times the number who are blind in both eyes as a result of injury have lost the sight of one eye from this cause. About half of blindness from injury occurs from occupational hazards and the rest at play or in the home. Industrial eye programs, in which the national society has cooperated with the Joint Committee on Industrial Ophthalmology, are aimed at elimination of unnecessary blindness from injury and also the discovery of and obtaining of treatment for persons who need eye care. A good industrial vision program should include:

1. Testing for the five basic visual skills.
2. Analysis of jobs for visual factors.
3. Eye safety equipment with correction for the job.
4. Specific provision for emergency eye care.
5. Proper use of illumination and color.
6. Group and individual education in eye health and safety.

Indirectly an industrial vision program is focusing the attention of a large segment of our population, otherwise difficult to reach, on the value of eyesight. For example, in plants where there are chapters of the Wise Owl eye safety incentive club there is greatly increased interest on the part of employees in taking care of not only their own eyes but also those of their wives and children.

Among children in schools for the blind there was a 25 per cent decrease in blindness from eye injuries in 1948 as compared with 1936. This drop is attributed partly to wise legislation which has been adopted in 10 states to regulate the use of air rifles by children and in 29 states to control the sale of fireworks. Much additional educational work has been done by such persons as public health nurses who deal directly with mothers of young children. A recent study [3] of eye accidents among school children over a period of 17 years indicates that approximately 88,000 such injuries requiring medical attention occur each year and that about 1,000 children are losing the sight of at least one eye each year. In this group over half of the eye injuries occur during unsupervised play, and boys have three times as many injuries as do girls. The study reveals the need for greater concerted action by all agencies to educate children and parents concerning the importance of eyesight and the ways of eliminating eye hazards.

GLAUCOMA

Glaucoma, which is responsible for about one eighth of blindness in this country, is likely to be an increasing problem as public health measures increase the span of life. In 1900, seventeen per cent of the population was 45 years of age or older, and in 1960 census estimates predict that 33 per cent will be in this age group where glaucoma becomes so important.

Treatment for glaucoma is not satisfactory, and much research is needed to explore the fundamental causation, methods of diagnosis and prevention of loss of useful sight. However, in the light of what is now known, much can be done to reduce blindness from glaucoma. Early diagnosis and adequate treatment increase the likelihood of preventing loss of vision. Gradle [4] demonstrated how both effective medical social service interpretation to the patient of the nature of his condition and follow-up will result in better continuing care.

Of considerable interest is the case-finding study carried on in Philadelphia with nearly 4,000 department store and insurance company employees, among

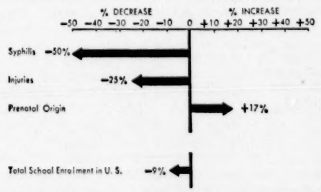

Fig. 1.—Trends in causes of blindness in the school age group from 1935-1936 to 1947-1948. Unit groups included are those for which data are available for both years. Data cover cases from 18 states (Kerby [3]).

whom 76 proved cases of glaucoma were found.[5] All of these cases were early, with no symptoms and fortunately with little visual field loss. This suggests an incidence of 2 per cent among men and women over 40 years of age and illustrates the need for routine tonometry on patients in this group. Further glaucoma case-finding studies now are in progress by the Detroit Society for the Prevention of Blindness and by the Richmond, Va., Department of Health.

CATARACTS

Cataracts are now responsible for about one fifth of all blindness. In over three quarters of these persons the lens opacities are those associated with the aging process and are commonly referred to as senile cataracts. In view of this popular terminology it is interesting to note the age distribution at onset of blindness for over 4,000 patients blind from cataracts.[6]

3. Kerby, C. E.: Eye Accidents to School Children, Sight-Saving Rev. **20**: 11 (Spring) 1950.
4. Gradle, H. S.: Glaucoma Errors That I Have Made and That I Have Seen, South. M. J. **33**: 498 (May) 1940.
5. Carpenter, E. M.; Brav, S. S., and Seidel, V. I.: Experiment in Glaucoma Case Finding, Am. J. Ophth. **33**: 611 (April) 1950, and personal communication to the authors.
6. Hurlin, R. G.; Saffian, S., and Rice, C. E.: Causes of Blindness Among Recipients of Aid to the Blind, Bureau of Public Assistance, Social Security Administration, Federal Security Agency, United States Government Printing Office, 1947.

Figure 2 shows that there were just about as many who became blind in the 50 to 59 age group as in the 60 to 69 group. In studying the records of persons blind from cataracts, one finds that the examining eye physician had recommended treatment for more than one half of them. Had surgery been performed it would have been possible to restore useful vision to a large proportion. These data suggest the need for general education and for public health nursing and medical social service which will help the person with cataracts to receive proper care.

FUTURE NEEDS

In a brief review of the causes of blindness, it becomes apparent that it is sometimes possible to prevent blindness by elimination of the cause—as in prevention of smallpox by vaccination, ophthalmia neonatorum by prophylactic procedures and injuries by enforcement of protective legislation and the wearing of safety glasses. Accomplishment of these measures requires general public education. As in many other medical fields, public education is also necessary to make the average man realize that even an apparently minor symptom may be the only warning he will have of a serious eye condition. The American public is eager for information on every medical subject. Misinformation is readily supplied by quacks and by some advertisers. Too often the result of such misinformation is delay and confusion in seeking and following sound professional advice. An important function of a voluntary health agency is to present authentic information on all subjects in its field. As the advertisers have demonstrated, repetition, human interest and forcefulness are required to make the message heard.

Case finding and case follow-up are preventive services discussed already in relation to glaucoma. Such activities also are of value in prevention of blindness from other eye diseases and will be more fruitful as treatment methods improve. In furnishing some of these preventive community services, we have sometimes found volunteer assistants of great help. Because of the importance of good vision in education, schools are usually eager to adopt vision-screening programs so that children with possible visual defects may be referred for eye care. With the cooperation of several other agencies,[7] the National Society has sponsored a research study of eye conditions among school children; one of the results of this study will be to indicate the best possible procedures for selection of children for referral. It is the purpose of such screening tests not to provide a diagnosis but simply to find those children probably needing eye care. The society also has been concerned with health and educational services for children still visually handicapped after receiving the best possible care, and it has led the fight to have partially seeing children provided for in regular school systems rather than segregated in schools for the blind.[8]

Both fundamental laboratory research and clinical research in the blinding eye diseases are urgently the best possible procedures for selection of children in schools for the blind, at least 16 per cent have hereditary conditions and 45 per cent are blind from other causes of prenatal origin.[9]

Although retrolental fibroplasia now accounts for the affliction of only 1.5 per cent of the children in schools for the blind, this condition undoubtedly will become increasingly prominent unless its causation can

TABLE 2.—*Causes of Blindness by Site and Type of Affection**

Site and Type of Affection	Percentage of Total, All Ages (Est.)
Eyeball in general	25.8
Glaucoma	11.6
Other	14.2
Cornea	13.9
Iris and ciliary	7.3
Crystalline lens	19.2
Cataract	18.8
Other	0.4
Choroid and retina	13.6
Optic nerve, visual pathway and cortical visual centers	17.7
All other and not specified	2.5

* Based on data from same source as that in table 1.

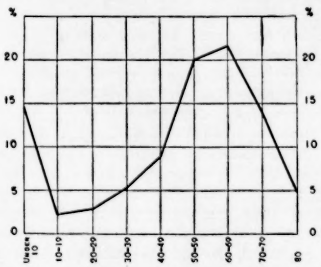

Fig. 2.—Distribution of blind due to cataract by age at onset of blindness. Data are from Social Security Board study, 20 states.[6]

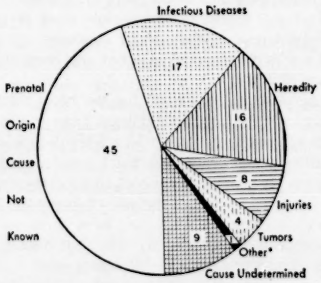

Fig. 3.—Causes of blindness in children of school age, based on 3,905 eye examination records of pupils in 39 residential schools and 20 city school systems in 35 states and the District of Columbia. Other * causes include general diseases and poisonings.

7. Children's Bureau, Federal Security Agency, Washington University College of Medicine, Missouri State Division of Health, St. Louis Board of Education.

8. Hathaway, W.: Education and Health of the Partially Seeing Child, New York, Columbia University Press, 1947.

9. Kerby, C. E.: Causes and Prevention of Blindness in Children, Sight-Saving Rev. **20**: 111 (Summer) 1950.

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be discovered and satisfactory methods of prevention or treatment found. Among adults, the cause of 70 per cent of cataracts and of 95 per cent of glaucomas was recorded by the examining ophthalmologist as unknown to science.

The recent war showed again what great strides can be made in scientific research when adequate funds are available and forces are mobilized under the most competent auspices. In a survey last year by the national society, heads of departments of ophthalmology in medical schools and eye institutes throughout the country reported the utter inadequacy of funds and their conviction that far more research was clearly indicated. We found that medical schools and other nongovernmental agencies had $546,894 and that various government agencies and departments had $365,840, or a total of under $1,000,000, for research in ophthalmology in the United States.

Because of these facts, the national society agreed last year to expand its aid to scientific research, which previously had been relatively small, and enlarged its committee on research in order to insure wise use of resources that may become available. The organization does not intend to carry on medical research but intends to raise funds on a far larger scale than ever before in order to make them available to those eye institutes, medical schools, eye clinics and laboratories where there is need for money and where intelligent use of grants can be assured. The success of other medical or health campaigns for funds encourages the society to believe that more can be accomplished in the battle against blindness during the next decade or two than has been done in our first half-century. The society, accordingly, is proceeding with an all-out unified campaign to reduce unnecessary blindness through supporting (1) basic and clinical research in the blinding eye diseases, (2) educational activities and (3) preventive services, including early case finding and case follow-through.

Because of close ties developed during the past 42 years with agencies and persons all over the United States, the National Society for the Prevention of Blindness is in a unique position today to unite all professional and lay groups interested in the fight to save sight. It already has more than 42,000 members and contributors in the 48 states and has affiliate societies in many state and local areas. Although there are over 600 organizations concerned with one or another aspect of blindness, the society is the only truly national organization making a total effort to eliminate unnecessary blindness. In 1948 the American people spent [10] large sums for the following products:

Over-the-counter eye lotions	$ 2,625,000
Eye Cosmetics	5,095,000
Over-the-counter headache relievers	101,510,000
Candy and chewing gum	1,854,548,000
Tobacco products and supplies	4,124,467,000
Alcoholic beverages	8,800,000,000

We believe that the American people will support a properly organized, well guided and forcefully presented effort to reduce blindness. In this work we shall need the help of every man and woman truly interested in promoting eye health for America.

ABSTRACT OF DISCUSSION

DR. WILLIAM L. BENEDICT, Rochester, Minn.: The National Society for the Prevention of Blindness merits warm commendation for its accomplishments. A lay organization with more than 40 years of distinguished service, it has endeavored to implement the resources of science and to strengthen the hand of the medical profession in the application of those principles of health and accident prevention throughout the world. Its chief function has been concerned with prevention of blindness, and its first field of endeavor was to encourage the universal application of recently discovered treatment of ophthalmia neonatorum, at that time a major cause of blindness. The scope of activities of the society is not so widely known among ophthalmologic circles as is deserved. The campaign against the scourge of blindness has been a labor of love by those who have devoted the major part of a lifetime to save thousands of children and adults from the tragedy of lifelong darkness. Drs. Lancaster and Foote have pointed out the requirements essential for an expanded program—basic and clinical research, educational activities and personnel for field services—and I wish to urge the necessity of support from this Section of Ophthalmology and from all other national, state and regional societies working for the ultimate objectives of this humanitarian movement. The society is organized on a nationwide basis and has affiliated with it several state societies. It is managed by an impartial board of directors, whose interests in medical, social and industrial fields bring to the work of the organization the wisdom and experience essential for economic administration and for undertaking of big jobs with assurance of their being carried to completion. The training of teachers, nurses and field workers is sponsored by the society, as are the surveys of industrial eye hazards and of the protective devices and safety measures recommended for use in mines, factories and on farms. The benefits of this service are of immense economic proportions, and their over-all value is immeasurable. In late years the problems of glaucoma are being intensively investigated; the study of maternal disease and its influence on the development of congenital cataract was inaugurated in cooperation with pediatricians; in fact, all causes of blindness have the attention of the National Society for the Prevention of Blindness, and its staff is being augmented as rapidly as facilities and financial support become available. The society now is planning aid to medical science by financial assistance in basic and clinical research. Its program has the endorsement and support of teachers and research workers throughout the nation. A fund-raising campaign has been endorsed by a well known agency after a careful scrutiny of the soundness of the purposes for which the proposed funds are to be used and of the organization as a disposing agency. Individual practitioners of ophthalmology should learn more of the work of this society. As members of state and county groups we should take advantage of the opportunities afforded by affiliation with the national societies for greater returns from our professional efforts and financial support. The need for expanded effort in the field of blindness prevention has been conservatively stated by Dr. Lancaster and Dr. Foote.

DR. M. HAYWARD POST, St. Louis: The most interesting development reported today is that a recent movement has been started by the National Society for the Prevention of Blindness to expand its aid to scientific research and that, in order to carry out this program to the best advantage, the society has materially enlarged its research committee. Undoubtedly, with proper organization and sufficient financial backing, much can be accomplished toward the better understanding of glaucoma and other diseases which are responsible for a great deal of blindness. Very wisely, the national society has felt that this work should not be carried on by the organization itself but that such funds as may become available should be allocated directly to eye institutions, clinics, laboratories and medical schools, where it is believed the money will be used most judiciously. Such funds are not as yet in hand, but it is unthinkable that they cannot be raised

10. Rennick, D.: Drug Topics Reports Trends in Sales of 141 Products, Drug Topics **93**:1 (Sept. 26) 1949.

when one considers the need, to say nothing of the economic value which would most certainly accrue to any reduction in the number of blind persons now requiring the expenditure of $50,000,000 a year. Surely it is true, in this instance, that "an ounce of prevention is worth a pound of cure." The National Society for the Prevention of Blindness is a logical instrument to carry out such a program. Its 42,000 members and contributors, distributed throughout the entire United States, and its close liaison with many local societies, both those devoted entirely to prevention of blindness or sight conservation and those working with the blind, seem to be assets which no other organization possesses and which should not be discarded. The record of the national society, furthermore, surely justifies confidence in its ability to give an excellent performance in the future, even as it has in the past. Since its founding 42 years ago it has been largely responsible for a 90 per cent reduction in blindness from ophthalmia neonatorum, as the result of a campaign for public education and support of legislation providing for the use of silver nitrate in the eyes of the newborn. To this might be added a reduction of 50 per cent in bindness since 1936 resulting from a like campaign concerning venereal disease. Another notable achievement has been the promotion of sight-saving classes, now 653 in number, with an enrolment of approximately 8,000 children. Less spectacular efforts have been those resulting in better eye hygiene in schools, better preparation of teachers in understanding sight-saving class work, social service work in eye clinics and the establishment of the first demonstration glaucoma clinic anywhere, along with many other notable contributions of enormous value. The National Society for the Prevention of Blindness is in an excellent position to carry through a campaign of public education, leading to the raising of funds on a nationwide scale for the support of eye research. I therefore appeal to all ophthalmologists to lend their support to the laudable efforts of this organization.

CLINICAL NOTES

CORTISONE IN SYDENHAM'S CHOREA

Report of Two Cases

Natalie Aronson, M.D.
Harold S. Douglas, M.D.
and
J. M. Lewis, M.D., New York

Beneficial effects of cortisone and pituitary adrenocorticotropic hormone (ACTH) on acute manifestations of rheumatic fever have recently been described.[1] In particular, the effects on rheumatic polyarthritis and carditis have been studied. Since acute chorea is generally believed to be another manifestation of rheumatic fever,[2] we considered it of interest to determine the effects of cortisone in two cases of chorea that have recently come under our observation. To one of the patients pituitary adrenocorticotropic hormone was also administered.

From the Department of Pediatrics, Beth Israel Hospital.
Aided by a grant from Loyal League for Philanthropies, Inc.

1. (*a*) Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: Effects of Cortisone Acetate and Pituitary ACTH on Rheumatoid Arthritis, Rheumatic Fever and Certain Other Conditions, Arch. Int. Med. **85**: 545 (April) 1950. (*b*) Thorn, G. W., and others: The Clinical Usefulness of ACTH and Cortisone, New England J. Med. **242**: 824 (May 25) 1950. (*c*) Massell, B. F.; Warren, J. E.; Sturgis, G. P.; Hall, B., and Craige, E.: The Clinical Response of Rheumatic Fever and Acute Carditis to ACTH, ibid. **242**: 641 (April 27); 692 (May 4) 1950. (*d*) McEwen, C.; Bunim, J. J.; Baldwin, J. S.; Kuttner, A. G.; Appel, S. B., and Kaltman, A. J.: Effect of Cortisone and ACTH on Rheumatic Fever, Bull. New York Acad. Med. **26**: 212 (April) 1950.

2. Sutton, L. P., and Dodge, K. G.: The Relation of Sydenham's Chorea to Other Rheumatic Manifestations, Am. J. M. Sc. **195**: 656 (May) 1938. Jones, T. D., and Bland, E. F.: Clinical Significance of Chorea as a Manifestation of Rheumatic Fever, J. A. M. A. **105**: 571 (Aug. 24) 1935.

3. Randolph, T. G.: Differentiation and Enumeration of Eosinophils in the Counting Chamber with a Glycol Stain, J. Lab. & Clin. Med. **34**: 1696 (Dec.) 1949.

REPORT OF CASES

CASE 1.—J. S., a 3 year old boy, was admitted to Beth Israel Hospital on June 18, 1950. Four weeks previously he had experienced a gradual onset of weakness of both arms and legs, associated with uncontrollable, purposeless movements of his limbs and face. Difficulty in swallowing and in speaking followed, and the patient was unable to sit or stand without support. Two weeks prior to admission, temperature of 101 F. and erythema multiforme, which lasted for two days, developed. The erythrocyte sedimentation rate at this time was 38 mm. in one hour (micromethod). No arthritis or other rheumatic manifestation was noted. The past history was not remarkable, and chorea and rheumatic fever had never been present in other members of the family.

On physical examination the patient was a well developed, well nourished 3 year old white boy who displayed almost continuous uncontrolled, purposeless movements of the limbs and trunk and frequent facial grimacing. His speech was nasal and unclear. The patient was unable to sit or stand because of marked weakness, which was more pronounced on the right side of his body. The hand grips were weak and unsustained. Meningitic signs were absent. The deep reflexes were equal and active, and a "hang-up" reflex was obtained when the right patellar reflex was elicited. The pharynx was normal. The heart did not appear enlarged, and there was a very soft systolic murmur at the apex which was not transmitted. Sinus rhythm was regular, with a ventricular rate of 88 a minute. The blood pressure was 110/80. The weight was 35 pounds (15.9 Kg.). The remainder of the physical examination revealed no abnormalities.

During the first four days in the hospital, generalized weakness persisted, while the choreiform movements decreased slightly but were still moderately severe. Cortisone therapy was begun on the fourth day in the hospital, with the following dosage schedule: 100 mg. daily for three days, followed by 50 mg. daily for six days. Since no definite improvement was noted at the end of that time, doses of cortisone were increased to 75 mg. a day for the next five days. The total dose in 14 days was 975 mg. The patient's clinical status was essentially unchanged throughout this two week period of cortisone administration.

A summary of the laboratory data may be found in chart 1. The results of laboratory studies before the institution of therapy were as follows: The urine was normal. The red blood cell count was 3,360,000 per cubic millimeter. The hemoglobin value was 11 Gm. per 100 cc. The white blood cell count was 9,850 per cubic millimeter, with 54 per cent polymorphonuclear leukocytes, 3 per cent staff forms, 40 per cent lymphocytes and 3 per cent monocytes. Eosinophils (direct count with the Randolph method)[3] were 75 per cubic millimeter. The erythrocyte sedimentation rate (Westergren method) was 3 mm. in one hour. Blood analyses (milliequivalents per liter) showed sodium concentration to be 141.5, chloride 105.7, potassium 5 and carbon dioxide-combining power 23. A 24-hour urinary excretion of 17-ketosteroids was 1.8 mg. A nose and throat culture revealed Neisseria (Micrococcus) catarrhalis and diphtheroids. The antistreptolysin titer was more than 2,000 units (normal, less than 200 units). The chest roentgenogram showed the cardiac silhouette to be globular but not enlarged. The electrocardiogram was interpreted as normal.

The laboratory determinations during therapy, June 22 to July 5, 1950, provided the following data: No changes were observed in the urine or in the concentration of erythrocytes, hemoglobin, leukocytes or eosinophils in the blood. The erythrocyte sedimentation rate, the carbon dioxide-combining power, and concentrations of sugar, sodium, chloride and potassium in the blood also remained normal. On the other

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hand, the urine 17-ketosteroids rose from 1.8 mg. (in 24 hours) to 4.3 mg. Electroencephalograms taken on June 28 and July 6 were both interpreted as normal.

CASE 2.—M. R., a 9 year old white boy, was admitted to Beth Israel Hospital on June 21, 1950. He had been entirely well until five days before admission, at which time he was

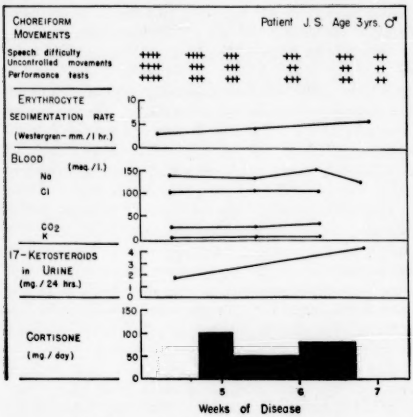

Chart 1 (case 1).—Summary of laboratory data.

noted to have purposeless movements of both arms and legs and facial grimaces. Difficulty in walking and in writing followed. No speech abnormalities were noted. There was no fever, arthralgia or other complaint. There was no past history of any rheumatic manifestation and no family history of chorea or rheumatic fever.

At the time of admission, the patient was noted to be a well developed, well nourished 9 year old boy, with moderately severe choreiform movements of all extremities, purposeless movements of his body and frequent facial grimacing. There was weakness of grip in both hands and an inability to button his clothes. The patient's speech and handwriting appeared normal. The deep reflexes were equal and active. Meningitic signs were absent. Examination of the heart revealed a faint short systolic murmur at the apex which was not transmitted. The ventricular rate was 80 a minute, with a regular sinus rhythm. The blood pressure was 100/80. The weight was 56 pounds (25.4 Kg.). The remainder of the physical examination disclosed no abnormalities.

On the fourth day in the hospital, erythema multiforme developed, with lesions over the buttocks, upper part of the back, upper part of the trunk, knees and elbows. These lesions changed in appearance and distribution in eight to 10 days and then disappeared completely. During this period the patient remained afebrile, although the erythrocyte sedimentation rate was elevated, ranging between 27 and 45 mm. in one hour (Westergren).

Cortisone therapy was started on the ninth hospital day: 150 mg. on the first day, 100 mg. on the second day and thereafter 50 mg. a day for four days. Since no clinical improvement was noted at the end of that period, doses were increased to 100 mg. a day and were maintained at that level for the following six days. Despite the increase in doses, the symptoms became severer; e. g., difficulty in writing became worse, and difficulty in speaking appeared for the first time. Doses of cortisone were then increased to 150 mg. a day and were administered in this amount for an additional seven and one-half days. By the end of this 20 day period a total of 2.175 Gm. of cortisone had been given, but the symptoms of the chorea, nevertheless, had become progressively more intense.

The use of pituitary adrenocorticotropic hormone was started on the day that administration of cortisone was discontinued, the dosage being 25 mg. every six hours intramuscularly. The drug was given for nine days, and the total dosage was 0.925 Gm. During this time there occurred a gradual but slight improvement of symptoms. However, the improvement was not striking, and at the conclusion of therapy with this drug mild to moderate chorea was still present.

A summary of the laboratory data appears in chart 2. The laboratory studies on admission revealed the following facts: The urine was normal. The red blood cell count was 3,410,000 per cubic millimeter. The hemoglobin value was 10.5 Gm. per 100 cc. The white blood cell count was 13,250 per cubic millimeter, with 73 per cent polymorphonuclear leukocytes, 2 per cent staff forms, 24 per cent lymphocytes and 1 per cent monocytes. The erythrocyte sedimentation rate was 32 mm. in one hour. Blood analyses (milliequivalents per liter) showed the sodium concentration to be 148, chloride 106.5, potassium 5.6, and carbon dioxide-combining power 24.7. The blood glucose was 84 mg. per 100 cc. The antistreptolysin titer was over 1,000 units. The nose and throat culture revealed nonhemolytic streptococci, Staphylococcus albus and a Streptococcus of the viridans group. A 24-hour urinary excretion of 17-ketosteroids was 3.5 mg. Chest roentgenograms showed no cardiac abnormalities. The electrocardiogram and electroencephalogram were within normal limits.

Results of laboratory studies during cortisone administration, June 30 to July 19, 1950, were as follows: No changes were observed in the urine or in the concentrations of erythrocytes, hemoglobin or leukocytes in the blood. The blood concentrations of sugar, sodium, chloride and potassium and the

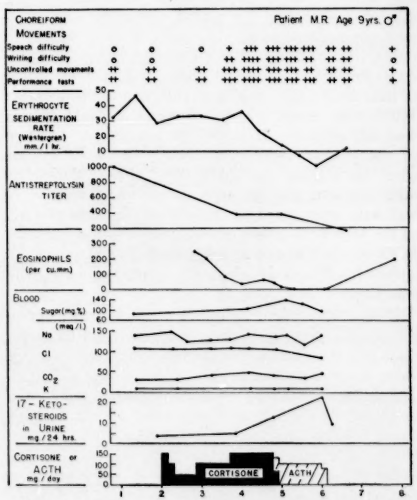

Chart 2 (case 2).—Summary of laboratory data.

carbon dioxide-combining power remained normal. Blood eosinophils fell from 263 per cubic millimeter on July 6 to 62 per cubic millimeter after 18 days of cortisone therapy. The erythrocyte sedimentation rate, which was 34 mm. in one hour on July 3, fell gradually to 19 mm. in one hour on July 18. The antistreptolysin titer fell to 400 units on July 13. The urine 17-ketosteroids on July 12 were 5 mg. (in 24 hours) and on July 18 were 11.9 mg. The electrocardiogram on July 7 was interpreted as normal. Electroencephalogram on

10 showed quantitatively less electrocortical activity than the previous record.

Laboratory studies during administration of pituitary adrenocorticotropic hormone, July 19 to July 28, revealed the following changes: The eosinophil count fell from 62 per cubic millimeter on July 18 to zero during therapy (on July 24 and 28). The erythrocyte sedimentation rate fell from 19 mm. in one hour on July 18 to 2 mm. in one hour after eight days of therapy. The antistreptolysin titer remained at 400 units July 21. The urine 17-ketosteroids rose from 11.9 mg. (in 24 hours) on July 18 to 23.6 mg. on July 27. The electroencephalogram of July 28 showed slightly slower activity than was present on the previous record.

COMMENT

Cortisone was administered to two patients with Sydenham's chorea and did not appear to influence the course of the disease in either case. The first patient, J. S., had chorea for four and one-half weeks before treatment and was given a total dose of 0.975 Gm. of cortisone over a period of two weeks. Slight to moderately severe chorea was still present at the time of discharge, which was seven weeks after the onset of symptoms.

The second patient, M. R., had chorea for only two weeks before cortisone therapy was begun. During the three weeks of treatment with cortisone the symptoms of chorea became much worse, despite the administration of comparatively large doses (150 mg. daily). Slight improvement was noted during the subsequent nine day period of therapy with pituitary adrenocorticotropic hormone, a total dosage of 0.925 Gm. (100 mg. daily) having been given. However, the child continued to have evidences of chorea of mild to moderate degree on cessation of this therapy. When seen again, 12 days later, very mild chorea was still present. It is difficult to evaluate the role of the pituitary adrenocorticotropic hormone in this case, since there was no striking change during its administration and the slight improvement noted may well have represented the natural course of the disease, as the average duration of chorea of moderate severity is six to eight weeks and this child had been ill with chorea for five weeks when administration of the drug was begun.

In this connection, it may be of interest to mention the recent report of Massell,[1c] who expressed the belief that pituitary adrenocorticotropic hormone was of value in the treatment of chorea in a 7 year old child. The dosage of the drug which he employed was 30 mg. daily for a period of nine days (and 10 mg. for one day), corresponding to a total dosage of 0.280 Gm. However, it must be emphasized that the therapy was begun during the sixth week of illness, and it may well be that the favorable course was unrelated to therapy. The evaluation of any treatment in chorea is exceedingly difficult and is particularly so when therapy is not given early in the course of the disease.

There were no signs of hyperadrenalism observed during the use of cortisone or pituitary adrenocorticotropic hormone in our patients. Weights did not change appreciably. Mental changes were not noted, but the appetites of both patients definitely improved. With regard to other physiological effects of these hormones, the following changes were observed: The urine 17-ketosteroids in case 1 rose from 1.8 mg. (in 24 hours) before therapy to 4.3 mg. after two weeks of cortisone therapy. In case 2 the urine 17-ketosteroids gradually increased from 3.5 mg. (in 24 hours) before treatment to 11.9 mg. after 18 days of cortisone therapy and to 23.6 mg. after administration of pituitary adrenocorticotropic hormone for seven days. The eosinophil counts in case 2 fell gradually during cortisone administration (263 to 62 per cubic centimeter) and fell precipitously with pituitary adrenocorticotropic hormone therapy (62 to 0 per cubic centimeter).

The electroencephalograms of these patients are of interest. Four electroencephalograms were taken of patient M. R.: one before therapy, one during cortisone administration, one during pituitary adrenocorticotropic hormone administration and one after medication had been discontinued for 12 days. The initial record was normal. The tracing taken after 10 days of cortisone therapy showed reduced electrocortical activity. The tracing taken after nine days of pituitary adrenocorticotropic hormone therapy showed even more pronounced slowing of activity. The final record, 12 days after cessation of this therapy, was again normal. Electroencephalographic abnormalities of the type noted here have been described as accompanying administration of pituitary adrenocorticotropic hormone [4] and also as occurring during acute chorea.[5] It is therefore not clear whether the changes described in this patient were the result of therapy or the result of the disease. The former possibility appears more likely, since the abnormal tracings were noted only during therapy and were preceded and followed by normal records. In contrast to the above, the two electroencephalograms of patient J. S., taken during the administration of cortisone, were within normal limits.

Both of our patients were considered to have acute rheumatic fever because of the association of acute chorea with an elevated erythrocyte sedimentation rate and erythema multiforme. In view of the effectiveness of cortisone and pituitary adrenocorticotropic hormone therapy in decreasing the elevated sedimentation rate of active rheumatic fever, it is interesting to note that in case 2 the sedimentation rate fell simultaneously with a worsening of the chorea. It appears that the two drugs, in contrast with their beneficial effects on certain rheumatic manifestations, do not favorably influence at least one rheumatic manifestation—that is, chorea. However, the possibility exists that with larger doses than are now generally employed the use of either drug may yet prove to have a beneficial effect on chorea. Further experiments are necessary to investigate this possibility.

SUMMARY

Two children with acute chorea were treated with cortisone and failed to show a favorable response. The total dosage of cortisone administered was 0.975 Gm. over a 14 day period in case 1 and 2.175 Gm. over a

4. Hoefer, P. F. A., and Glaser, G. H.: Effects of ACTH Therapy, J. A. M. A. **143**: 620 (June 17) 1950. Buchanan, D. M.; Walker, A. E., and Case, T. J.: The Pathogenesis of Chorea, J. Pediat. **20**: 555 (May) 1942.

5. Usher, S. J., and Jasper, H. H.: The Etiology of Sydenham's Chorea: Electroencephalographic Studies, Canad. M. A. J. **44**: 365 (April) 1941.

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20 day period in case 2. In one of these cases the patient was subsequently treated with 0.925 Gm. of pituitary adrenocorticotropic hormone (ACTH), given over a period of nine days. It was considered that the slight improvement noted during the administration of the drug was probably unrelated to therapy.

COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

Ascorbic Acid (See New and Nonofficial Remedies 1950, page 469).

The following dosage form has been accepted:

Tablets Ascorbic Acid: 50 mg. and 100 mg. Sutliff & Case Company, Inc., Peoria, Ill.

Heparin Sodium-U.S.P. (See New and Nonofficial Remedies 1950, page 301).

The following dosage form has been accepted:

Liquaemin Sodium (High Potency): 1 cc. ampuls. A solution containing 5,000 U.S.P. units (approximately 50 mg.) of heparin sodium in each cc. Preserved with 0.45 per cent phenol. U. S. trademark 361,309. Organon, Inc., Orange, N. J.

Meth-Dia-Mer-Sulfonamides (See New and Nonofficial Remedies 1950, page 127, Sulfadiazine-Sulfamerazine-Sulfamethazine Mixture).

The following dosage form has been accepted:

Suspension Trionamide with Sodium Citrate: 60 cc., 473 cc. and 3.78 liter bottles. A suspension containing 33 mg. each of sulfadiazine, sulfamerazine and sulfamethazine and 66 mg. of sodium citrate in each cc. Flint, Eaton and Company, Decatur, Ill.

Penicillin for Injection for Prompt Action (See New and Nonofficial Remedies 1950, page 141, Penicillin for Parenteral Use in Aqueous Solution).

The following dosage form has been accepted:

Crystalline Potassium Penicillin G (Buffered): 100,000, 200,000, 500,000, 1,000,000, 2,000,000 and 5,000,000 unit vials. Buffered with 4.5 per cent sodium citrate. Lederle Laboratories, Pearl River, N. Y.

Penicillin for Inhalation (See New and Nonofficial Remedies 1950, page 139, Penicillin for Inhalation or Oral [Sublingual and Pediatric] Administration).

The following dosage form has been accepted:

Powdered Crystalline Potassium Penicillin G: 100,000 units in sifter cartridges for use in Aerohalor. Abbott Laboratories, North Chicago, Ill.

Sulfadiazine-U.S.P. (See New and Nonofficial Remedies 1950, page 122).

The following dosage form has been accepted:

Tablets Sulfadiazine: 0.5 Gm. Physicians' Drug and Supply Company, Philadelphia.

Pyridoxine Hydrochloride (See New and Nonofficial Remedies 1950, page 485).

The following dosage forms have been accepted:

Solution Pyridoxine Hydrochloride: 2 cc. ampuls and 5 cc. vials. A solution containing 25 mg. of pyridoxine hydrochloride in each cc. The 5 cc. vial is preserved with 0.9 per per cent benzyl alcohol. Abbott Laboratories, North Chicago, Ill.

Tablets Pyridoxine Hydrochloride: 25 mg. and 50 mg. Abbott Laboratories, North Chicago, Ill.

Testosterone Propionate-U.S.P. (See New and Nonofficial Remedies 1950, page 360).

The following dosage forms have been accepted:

Solution Testosterone Propionate in Oil: 10 cc. vials, a solution in sesame oil containing 25 mg. of testosterone propionate in each cc. Preserved with 0.5 per cent chlorobutanol. Metropolitan Laboratories, Inc., Oyster Bay, N. Y.

Solution Testosterone Propionate in Oil: 1 cc. vials, a solution in cottonseed oil containing 10 mg. of testosterone propionate in each cc. 1 cc. and 10 cc. vials, a solution in cottonseed oil containing 25 mg. of testosterone propionate in each cc. 10 cc. vials, a solution in cottonseed oil containing 50 mg. of testosterone propionate in each cc. The 10 cc. vials are preserved with 0.5 per cent chlorobutanol. The Upjohn Company, Kalamazoo, Mich.

Thiamine Hydrochloride-U.S.P. (See New and Nonofficial Remedies 1950, page 488).

The following dosage form has been accepted:

Tablets Thiamine Hydrochloride: 1 mg. Sutliff & Case Company, Inc., Peoria, Ill.

COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION

REPORT OF THE COUNCIL

The Council on Physical Medicine and Rehabilitation has authorized publication of the following report.

HOWARD A. CARTER, *Secretary.*

SONOTONE SCREENING AUDIOMETER, MODEL 30, ACCEPTED

Manufacturer: Sonotone Corporation, Elmsford, New York.

The Sonotone, Model 30, Screening Audiometer is a portable, battery-operated, pure-tone audiometer designed primarily for use in the preliminary testing of children in schools or of other groups of persons. This audiometer is also made for 115 volt AC operation. It is designed for tests of air conduction only. The frequency range is from 250 to 8,000 cycles in octave steps, and the intensity range is from —10 db. to +60 db. of hearing loss. The instrument is contained in a metal box measuring about 15 by 43 by 18 cm. (6 by 17 by 7 inches) and weighing 5.4 Kg. (12 pounds). The shipping weight is 8.2 Kg. (18 pounds).

Sonotone Screening Audiometer, Model 30

Evidence from sources acceptable to the Council showed that the device was well constructed, performed as claimed by the manufacturer and satisfied the minimal requirements adopted for the acceptance of screening audiometers. The Council on Physical Medicine and Rehabilitation voted to include the Sonotone Screening Audiometer, Model 30, in its list of accepted devices.

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OF THE AMERICAN MEDICAL ASSOCIATION
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Associate Editor . . . . . JOHNSON F. HAMMOND, M.D.
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A NEW FACE FOR THE JOURNAL

This issue of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION reflects a number of changes intended to make it more readable and even more useful to its readers. For more than a year a file has been maintained for the collection and study of letters from readers who offered suggestions for improvement, commented favorably on some particular section or sections or criticized a department as being unnecessary or not particularly helpful. At the same time, a careful study was made of the reading habits of those who received THE JOURNAL or had access to it. A partial report on this study appeared in the report to the House of Delegates.[1] In addition, several experts in typography, journal layout and book makeup were consulted for their opinions. A few others, hearing of possible changes, volunteered their suggestions.

As a result of the study and suggestions, a number of basic changes were adopted with the hope and belief that these would be helpful to the readers and would meet even better the needs of the American Medical Association. THE JOURNAL is a scientific medical publication, and its main function is to present scientific medical information. However, it also is an organization journal and must contain material that is concerned directly or indirectly with the organizational activities of the American Medical Association. Thus, these two main functions had to be kept in mind as consideration was given to changes in appearance and makeup. Furthermore, since THE JOURNAL has for many years had a distinctive appearance, it was necessary to avoid drastic changes.

This issue carries to completion some of the changes that were introduced gradually during 1950. It also reflects other modifications that were proposed so willingly by the friends of THE JOURNAL and of the American Medical Association. The "new" journal is a composite of the proposals offered by those who have studied it over the past months. It does not reflect one person's thoughts, but many.

1. J. A. M. A. **144**: 633 (Oct. 21) 1950.

Paramount among the changes are a newly designed cover, which is intended to provide more information on the contents, and use of a new type, known as Times Roman. This type was cut in 1948 but already has received considerable recognition for use in periodicals published at frequent intervals. It is an easily read type, more open, blacker in appearance and, in general, restful to the eye. Other changes consist of the development of uniformity between departments and simplification of the style used. While these may or may not be particularly noticeable to many readers, they are of great importance to a publisher who must be concerned with cost. If a page can be set completely on one machine, it is much less expensive to do such setting than to have the page transferred to another or possibly two other machines because of the use of a type not available on the first machine. This changing involves an appreciable amount of handling, which over a year can become an expensive item. Even the setting of a heading flush with the left or right of a column is less time consuming and less expensive than centering it.

And so it is with the other changes that are not reported here in detail. Most will be readily apparent. The others will be apparent when more careful study is given to the pages. For example, the questions in Queries and Minor Notes are now set in italics, which again provides a more easily read page and at the same time is in keeping with modern journalism. The Washington News column, which since its inception has appeared before the Organization Section, has been moved to the advertising section in the front part of THE JOURNAL. Its location will always be identified on the cover, but the change was made for a number of reasons, one of them being to permit this column, which has become increasingly popular, to stand by itself, another being to direct more attention to the interesting information and helpful hints that so often appear in the advertising pages.

Much time has been spent in the development of the new format. It has been made possible because of the understanding and helpful attitude of so many friends of THE JOURNAL and of the American Medical Association who, without thought of personal gain, gave freely of their advice. To them much gratitude is owed. Suggestions have always been welcomed by the Editorial Department. They still are welcome, and it is the hope of every member of the Editorial Department and of the Board of Trustees, under whose auspices THE JOURNAL is published, that suggestions and criticism will continue to arrive from readers. Obviously, not all the suggestions can be adopted. Nevertheless, none are ever ignored and some, while not practical now, may be feasible in the future.

It has been exciting and pleasant to plan for the changes that have been made in THE JOURNAL. We hope you like them.

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DUES IN THE AMERICAN MEDICAL ASSOCIATION

In the Organization Section of this issue of THE JOURNAL is a list of questions and answers on the payment of dues in the American Medical Association. Because such payment is still a comparatively new procedure in the history of the Association, some confusion exists concerning the status of physician members who pay dues and those physicians who do not. The questions and answers which supply information on these and other problems have been prepared from questions reaching the office of the Secretary of the American Medical Association.

In 1951 for the first time members of the Association who pay their dues will receive THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION without additional payment. Fellows of the Association may elect to take one of the specialty journals if they desire instead of THE JOURNAL. This privilege is accorded only to Fellows. However, most members may become Fellows simply by making application to the Secretary of the American Medical Association and paying an additional sum of $5, the Fellowship dues.

Not infrequently a physician asks about the advantages of being a Fellow. It would be impossible to list all the advantages in an editorial. However, briefly summarized, those who hold Fellowship are permitted to hold office in the American Medical Association, can be elected as a delegate from their state medical association and can participate in the Scientific Assembly, which is "the convocation of its (American Medical Association) Fellows for the presentation and discussion of subjects pertaining to the science and art of medicine." Those who attend the meetings of the American Medical Association and who participate in the affairs of its scientific councils and committees know by personal experience what is meant by the words "presentation and discussion of subjects pertaining to the science and art of medicine." Fellowship indicates the additional interest of members who wish to advance by personal participation and support the scientific and organizational objectives of the Association to which they belong. This is the philosophy of and honor accorded to Fellows in any widely recognized scientific organization.

From time to time interested observers ask: What does a physician gain by being a member of the American Medical Association? Like trying to describe the advantages of Fellowship, this question is impossible to answer in the confines of any brief statement. Lengthy articles and booklets have been written and are available to any who wish to inquire for them. The Constitution and By-Laws of the American Medical Association, for example, contains a wealth of information on what accrues to Fellows and members of the Association. The issue of THE JOURNAL that contains the reports to the House of Delegates provides details on the many offices that make up the Association and that serve the medical profession and the nation. In fact, this service is reflected far beyond the boundaries of the United States, as many people in other countries follow the activities of the American Medical Association and put into practical application some of its findings and recommendations. The Oct. 21, 1950, issue of THE JOURNAL contains the reports that show what the Board of Trustees, the Secretary, the publication department, the Washington Office, the Public Relations Department, the scientific councils and the many other councils, committees and bureaus do during the course of a year. Whether the reader is interested in medical education, voluntary insurance plans, the development of a scientific program or health education, he can find information on what the Association is doing in these and other fields by referring to this issue of THE JOURNAL.

Some ask what is done with the dues collected by the American Medical Association from its members. This money, and any obtained from other sources, is used to support the many activities undertaken by the Association. The headquarters office alone employs more than 800 persons, many of these having advanced training in professional fields. Thousands of dollars are set aside to offset the loss incurred in the publication of the nine special journals that are offered as a service for those interested in the more specialized aspects of medical practice. More thousands are used to underwrite the Quarterly Cumulative Index Medicus, which has international recognition as a research tool. The Library is not an inexpensive project and provides much help to physicians who wish up-to-date information on medical topics or who are looking for guidance in the preparation of papers on some particular medical problem that has come to their attention. The Association must underwrite a loss of $70,000 on the recent edition of its indispensable American Medical Directory. Examination of any of the budgets of the councils, bureaus, committees and other departments of the American Medical Association would reveal the expenditures necessary to advance the health objectives of those who have grouped themselves together to form the Americaan Medical Association. The laboratories, for example, which test the various products submitted to the scientific councils cost approximately $100,000 a year to operate; the Council on Medical Education and Hospitals has been spending up to a quarter of a million dollars a year to advance medical education standards; the Council on Pharmacy and Chemistry, the Committee on Research, the Council on Physical Medicine and Rehabilitation and the Council on Foods and Nutrition alone have budgets amounting to approximately $300,000; health education costs the Association $175,000 a year; the Bureau of Investigation spends more than $20,000 to expose quackery, and the Bureau of Legal Medicine and Legislation requires more than $75,000. These figures do not include the cost of operation of the various other councils and departments, such as the department of Public Relations, the Washington Office of the American Medical Association, the Council on Industrial Health and the Bureau of Medical Economic Research. Nor do they reflect the

cost of holding meetings twice a year, and they do not reflect various administrative expenses, such as personal property tax, furniture and equipment depreciation, insurance, postage and legal fees.

Thus, when one asks, "What do I get for my dues?" he must not expect a brief explanation. The work of the Association cannot be described briefly. Members and prospective members can obtain without charge from the Association a copy of the Handbook, which describes simply the makeup of the American Medical Association, the work of its various departments and the service that these departments provide for members. Any one department, if used fully by the member, will more than repay him for the small amount of money spent in dues. For example, to choose just one department: The Bureau of Legal Medicine and Legislation provides information on, among other things, partnership agreements; hospital records—medicolegal aspects; income taxes; malpractice; medical practice acts; cults; expert testimony; trauma and disease; privileged communications; coroner and medical examiner systems; blood-grouping tests in disputed parentage; chemical tests for intoxication—legal aspects; workmen's compensation and occupational disease legislation; legislation of medical interest—federal and state; basic science laws; premarital and prenatal examination laws; roentgenograms—ownership; confidential communications; autopsies—consent; operations—consent; sterilization operations; artificial insemination; birth control—legal aspects; Constitution and By-Laws, and food and drug legislation. The Washington Office, as another example, provides information on federal legislation on health, bulletins on legislative matters and copies of specific bills.

It is no wonder that members of the American Medical Association pause for a moment when they are asked by patients or others: What do you get for being a member of the Association? There are so many ways in which they gain personally, for the profession as a whole and for the general population, that they have to pause if some semblance of order is to appear in the reply.

The American Medical Association is entering another historic year—historic in its own organizational activities and historic so far as the nation is concerned. Medicine has much to offer to this and other countries. On it depends the health of the people. The American Medical Association is determined to meet its responsibilities in the solution of health problems as they arise. This determination, however, can be carried completely to fruition only when active support is provided by its members, which means that physicians should be more than just passive members of the Association; they should be active participants in the affairs of the American Medical Association, their state medical association and their county medical society. The more active they are, the more readily they can answer the question: What do you get for your dues?

FORTIETH ANNIVERSARY ON HEALTH PROBLEMS IN EDUCATION

The year 1951 marks the fortieth anniversary of the founding of the Joint Committee of the American Medical Association and the National Education Association on Health Problems in Education. First created in 1911, at the suggestion of the American Medical Association, the Committee has been functioning continuously since that time, bringing together the appointed delegates of the professions of medicine and education. In general its function is to consider principles and policies and to make recommendations on problems of mutual concern affecting the health of school children and youth.

The most harmonious relations have been established between the two great associations. Without official formula it has become the custom to alternate the annual meetings of the Committee between the two headquarters offices in Chicago and Washington, D. C., and to alternate the chairmanship of the group between a physician and an educator. Interim activities are carried on by subcommittees, which invariably include representatives of both professions.

The Committee has a splendid history of achievement in soundly conceived health work. Its statements of principle and policy and the authoritative book "Health Education" reflect the combined viewpoint of medicine and education on school health matters. Over 40 publications, more than 20 of which remain pertinent and helpful, have set forth the recommendations of the Committee. These materials have found their way into the schools in every corner of the country and have strongly influenced the education of teachers and other school personnel. Many have been distributed outside the United States and some have been reproduced abroad.

The Joint Committee was instrumental in gaining official recognition of health as a major aim of education. Even more important, it has shared substantially in the contribution that health education has made to bettering the health of the nation. Scientific medical advances provide the means for improving the public health, but it remains for health education to motivate people to take advantage of medical progress. What better place than the schools to further this cause—to instill responsibility for one's own health and the health of others? What better place to provide accurate information, to teach right attitudes and to develop intelligent health practices?

With increasing knowledge in the fields of environmental sanitation and mental health there has come an awareness of the importance of school surroundings in promoting healthful living. More than physical factors of the environment, like good heating, lighting, ventilation and seating, are included; the mental-emotional climate is equally important. The health of teachers and other school employees, who are in inti-

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mate contact with children, is involved. Administrative policies, teaching technics and the organizational structure of the school also strongly influence the health of children.

When children are gathered together in the school, health problems are the inevitable result—problems of communicable disease, problems of emergency care for accidents and sudden illness, problems having to do with the physical activities of children, problems associated with the education of the handicapped and problems connected with the discovery, follow-up and correction of other health conditions that interfere with satisfactory school progress.

To solve these problems school health programs have been established; they will continue to be developed and expanded. If they are to be effective, if they are to take a desirable pattern, medical guidance is essential.

At the present time many schools are conducting good school health programs, but much remains to be done. The good work must be spread to all the schools in the nation. The work of the Joint Committee of the two great professions is important, but even more vital are the efforts of physicians and educators in local communities. A school health or other appropriate medical society committee, working with the school and health department officials, can encourage the growth of properly directed school health work. As in the past the Association will continue to cooperate with education at the national level. In the local communities individual physicians can be depended on to do their part.

CRIME AND PUNISHMENT

In a memorandum submitted to the Royal Commission on Capital Punishment, Sir David K. Henderson [1] expressed the opinion that the legal attitude with regard to crime is too greatly dominated by a moralistic point of view, by the concept of reason and free will and the lack of appreciation of the fact that conduct is motivated by instinctive drives that operate at a much less conscious level. The medical point of view, to the contrary, is too liberal in that it concerns itself too greatly with the individual and probably does not fully appreciate its duty to society. Be that as it may, Sir David insists that individualization is the dominant truth of modern medical science, whether applied to disease or to crime. The large army of recidivists, in his opinion, is probably the best answer to the legal methods at present in use.

Sir David believes that the plea of insanity in cases involving a capital charge is made too often. In cases of less serious type, on the contrary, the plea of mental disorder is not submitted often enough, largely because the accused would prefer to receive a defined prison sentence rather than undergo prolonged treatment in a mental hospital. The British courts, it appears, in testing the truth of the plea and mental disorder, follow the method used in the United States, allowing both the prosecution and the defense to submit independent medical evidence. Henderson stresses that, while it is often difficult, if not impossible, to define degrees of unsoundness of mind, there are types of mental disorder that should exonerate a person from a charge of criminal conduct. Such conditions are melancholia, schizophrenia, paranoid states, general paralysis, senile dementia, epilepsy with insanity and a number of others. In many of these cases the person's mind is sufficiently clear so that he knows what he is doing but the true significance of his conduct in relation to himself or to others is not appreciated. Henderson is of the opinion that persons who are proved to be insane in a medical sense are not legally responsible for the crime they may commit. Lord Justice Clerk Inglis was of the opinion that "in a strictly legal sense there is no insane criminal. The act of the insane, which in the sane would be criminal, lacks every element of crime."

The legalistic attitude is most in error in the refusal to allow mental deficiency to be utilized as defense. Such an outlook, in the author's opinion, is a grave injustice. A prison sentence in such cases had no deterrent or remedial effect. Persons of this type should be cared for under hospital or colony conditions until they can be discharged.

With regard to psychoneurotics the medical profession takes the attitude that the signs and symptoms which constitute their conduct disorders are determined at a subconscious or unconscious level and are the result of the constant conflict that exists between the good and the evil, between one's conscious and one's instincts. Some modern psychiatrists, the freudians in particular, would insist that all criminal acts must be determined on the basis of conflict and that the criminal person should be regarded as a sick person and not as a delinquent. Henderson thinks that this is an extreme view that would not be acceptable to most in the present state of our knowledge. He thinks that the conflict which produces criminal acts in the case of delinquents is much the same type as that which produces psychoneuroses.

The problems in the study of criminal conduct involve a consideration of genetic and environmental factors, such as housing, education and marriage. The more immediate and practical requirements are those of creation of psychiatric units for examination and observation of the criminal before trial and for adequate treatment after trial, an efficient after-care organization and the establishment of a special colony under psychiatric control. Henderson cites the Herstedvester Institution in Denmark as a model mental institution of that type.

1. Henderson, D. K.: Reflections on Criminal Conduct and Its Treatment, Brit. M. J. 2: 311 (Aug. 5) 1950.

ORGANIZATION SECTION

Information on Membership Dues

The following information on membership dues for the American Medical Association for 1951 has been compiled by the office of the Secretary of the American Medical Association. This has been made available through the Secretary's Letter by Dr. George F. Lull for officers of the American Medical Association and all county and state medical organizations. It is reproduced here for the interest of the readers of THE JOURNAL.

1. American Medical Association membership dues for 1951 are $25.

2. Fellowship dues for 1951 are $5 and are exclusive of membership dues.

3. American Medical Association membership dues are levied on "active" members of the Association. A member of a constituent association who holds the degree of Doctor of Medicine or Bachelor of Medicine and is entitled to exercise the rights of active membership in his constituent association, including the right to vote and hold office as determined by his constituent association, and has paid his American Medical Association dues, subject to the provisions of the By-Laws, is an "active" member of the Association.

4. American Medical Association membership dues are payable through the component county medical society or the constituent state or territorial medical association, depending on the method adopted locally.

5. Fellowship dues are payable directly to the headquarters of the American Medical Association, 535 North Dearborn Street, Chicago 10, on receipt of the bill for such dues.

6. A dues paying, active member is eligible for Fellowship and may request such status by direct application to the Secretary of the American Medical Association. Applications for Fellowship are subject to approval by the Judicial Council of the Association.

7. Commissioned medical officers of the United States Army, the United States Navy, the United States Air Force or the United States Public Health Service, who have been nominated by the Surgeons General of the respective services, and the permanent medical officers of the Veterans Administration, who have been nominated by its Chief Medical Director, may become Service Fellows on approval of the Judicial Council. Service Fellows need not be members of the component county or constituent state or territorial associations or the American Medical Association and do not pay Fellowship dues. They do not receive any publication of the American Medical Association except by personal subscription. If a local medical society regulation permits, a Service Fellow may elect to become an active member of a component and constituent association and the American Medical Association, in which case he would pay the same membership dues as any other active member and receive a subscription to THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

8. An active member of the American Medical Association may be excused from the payment of American Medical Association membership dues when it is deemed advisable by the Board of Trustees, provided that he is excused from the payment of full dues by his component society and constituent association.

The following may be excused in accordance with this provision: (*a*) members for whom the payment of dues would constitute a financial hardship as determined by their local medical societies; (*b*) members in actual training for not more than five years after graduation from medical school, and (*c*) members who have retired from active practice.

9. Active members of the American Medical Association are not excused from the payment of American Medical Association membership dues by virtue of their classification by their local societies as "honorary" members or because they are excused from the payment of local and state dues. Active members may be excused from the payment of American Medical Association membership dues only under the provision described in paragraph 8 above.

10. American Medical Association membership dues include subscription to THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. Active members of the Association who are excused from the payment of dues will not receive THE JOURNAL except by personal subscription at the regular subscription rate of $15 a year.

11. Member Fellows may substitute one of the specialty journals published by the Association for THE JOURNAL, to which they are entitled as members. A Fellow who substitutes a specialty journal will not also receive THE JOURNAL.

12. A member of the American Medical Association who joins the Association on or after July 1 will pay membership dues for that year of $12.50 instead of the full $25 membership dues.

13. An active member is delinquent if his dues are not paid by December 31 of the year for which dues are prescribed and shall forfeit his active membership in the American Medical Association if he fails to pay the delinquent dues within thirty days after the notice of his delinquency has been mailed by the Secretary of the American Medical Association to his last known address.

14. Members of the American Medical Association who have been dropped from the Membership Roll for nonpayment of annual dues can not be reinstated until such indebtedness has been discharged.

15. The apportionment of delegates from each constituent association shall be one delegate for each thousand (1,000), or fraction thereof, *dues paying active members of the American Medical Association* as recorded in the office of the Secretary of the American Medical Association on December 1 of each year.

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Scientific Exhibit, Atlantic City Session

Attention is called to the fact that applications for space in the Scientific Exhibit at the Atlantic City Session will close on Jan. 15, 1951. All applicants must fill in the regular application blank, giving the amount of space needed and a short description of the proposed exhibit. Applications received after the closing date will be placed on the waiting list to be considered by the Committee on Scientific Exhibit if space is available.

Applications for time on the motion picture program also close on January 15. Applicants should be prepared to send their films in for preview by the Committee on Medical Motion Pictures. Motion pictures will be shown in two rooms set aside for that purpose, and no films will be shown in exhibitors' booths. It is expected that each film will be shown once each day during the meeting, and it is hoped to have as many of the authors present to discuss the films as possible.

Application blanks for space in the Scientific Exhibit or for time on the motion picture program may be obtained from any of the Section Representatives or from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago 10.

New Board Members of World Medical Association

Robert B. Smallwood, president of Thomas J. Lipton, Inc., Carleton H. Palmer, president of E. R. Squibb & Sons, Inc., and James J. Kerrigan, vice president of Merck & Co., Inc., have been elected to the board of directors of the United States Committee of the World Medical Association. The United States committee is a nonprofit organization which aims to support the activities of the World Medical Association, an organization of the national medical association of 40 countries working to further medicine, health and peace throughout the world. The United States committee has guaranteed to underwrite the costs of the association's U. S. headquarters, the secretariat of the association located at 2 East 103rd Street, New York 29, as well as the cost of publishing *The World Medical Association Bulletin*. The board of directors, consisting of 25 men, is the governing body of the committee and entirely responsible for its activities.

GOVERNMENT SERVICES

ARMY

Increase in ROTC Enrolment.—Medical Reserve Officers Training Corps enrolment for the academic year 1950-1951 in the 48 medical schools participating in the program shows an increase of 18 per cent over last year's enrolment, according to Major Gen. R. W. Bliss, the Surgeon General. Sixty-eight per cent of the 4,888 medical ROTC students are veterans, which is a decrease of only 11 per cent from last year's ROTC enrolment of 4,148. Total ROTC enrolment in the 76 medical, dental, veterinary and pharmacy schools participating in the programs increased by 20 per cent, to 7,372 students. Pharmacy college units made the largest gain, 53 per cent, with 503 students this year, followed by veterinary schools, 20 per cent, with 530 students, and dental units, 19 per cent, 1,451 students. Veterans comprise 67 per cent of the total enrolment in the four categories, a decrease of only 9 per cent from the preceding year. Nonveterans exceed veterans only in the pharmacy corps units, where the ratio is 45 per cent for veterans.

Illinois National Guard Needs Physicians.—There are several openings for physicians and dentists who are able to qualify as commissioned officers in the 108th Battalion of the 33rd Division, Illinois National Guard. Men of draft age are being favorably considered for deferment if they are members of the National Guard.

Recent graduates whose draft status is uncertain should avail themselves of this opportunity to join the National Guard and assure themselves a commission.

The medical battalion meets on Wednesday nights from 8:00 to 10:00 p. m., for which one day's pay is given. Interested men can secure information by calling the Northwest Armory, EVerglade 4-1040, or by attending on any Wednesday night. The Armory address is 1551 North Kedzie Avenue, Chicago.

New Radiological Consultants Division.—Major Gen. R. W. Bliss, the Surgeon General, has announced the establishment of a Radiological Consultants Division in the Office of the Surgeon General. Col. Harold I. Amory (MC), chief of X-Ray Service, Walter Reed Army Hospital, Washington, D. C., has been named chief of the new division. He will continue in both posts. The new division will emphasize the diagnostic and treatment phases of clinical radiology, particularly with reference to cancer and allied diseases.

Personal.—Col. Warner F. Bowers (MC), chief surgical consultant, the Surgeon General's office, has been elected to the board of governors of the American College of Surgeons, succeeding Major Gen. Raymond W. Bliss, Surgeon General of the Army, whose term as a member of the board has expired.

NAVY

Disaster Unit Commended.—The personnel of the U. S. Naval Hospital, St. Albans, Long Island, N. Y., has been commended by Dr. Marcus D. Kogel, commissioner, New York City Department of Hospitals, for their aid in caring for survivors at the scene of the Thanksgiving Eve railroad accident in Queens, N. Y. Comdr. A. G. Simpson (MC) was placed in charge of one of the two first aid stations established at the scene by Dr. Kogel. Lieut. (jg) Emmett F. Ferguson (MC) was commended by Dr. Kogel for "the heroic work he performed at great personal hazard." Capt. Warwick T. Brown, commanding officer of the naval hospital, ordered three ambulances, seven doctors, eight nurses, one dental officer, one warrant officer HC, 10 corpsmen and a truckload of emergency medical supplies, including blankets and stretchers, to the scene. The hospital disaster and emergency unit remained in action nearly eight hours, until the last living survivor had been removed from the wrecked cars.

Dr. Rusk, Guest Lecturer.—Dr. Howard A. Rusk, New York, chairman, Health Resources Advisory Committee, National Security Resources Board, was the guest lecturer at the Naval Medical School, Bethesda, Md., December 8. His subject was "Medicine, Mobilization and Manpower."

Personal.—Rear Admiral Daniel Hunt (MC, USN) retired from the Navy December 1, after 37 years of active duty. Dr. and Mrs. Hunt now reside in Tacoma, Wash.

AIR FORCE

Dr. Selye Lectures at Aviation Medicine School.—Dr. Hans Selye, director, Department of Experimental Medicine and Surgery, University of Montreal. gave a series of lectures and seminars on stress physiology at the School of Aviation Medicine, Randolph Field, Texas, early in December. Dr. Selye, an internationally recognized authority on the endocrine glands, said, between his technical discussions, ". . . any kind of stress is of major importance to the Air Force. Stress of heat, cold, injury, anxiety or shock of any kind actually sets up chemical reactions or changes within the body which can cause serious ailments and even death." The layman's prescription given by Dr. Selye to reduce the medical technicalities of this problem to their least common denominator was "roll with the punch." "But how to do that," he added, "is one of the hardest things in the world to learn."

Personal.—Col. Charles E. Kossmann of New York City, a reserve officer, was ordered to three weeks' active duty at the School of Aviation Medicine to initiate revision of the "Flight Surgeon's Reference File," a manual that will be placed in the hands of every Air Force medical officer. Colonel Kossmann wrote the original "Flight Surgeon's Handbook" in 1942 and revised it in 1945. He graduated from the School of Aviation Medicine in 1941 and remained on duty there throughout the war.

PUBLIC HEALTH SERVICE

Meeting of Committee on Industrial Wastes.—Progress in organization for research on the disposal of industrial wastes that contribute to pollution of the nation's water resources will be reported to the National Technical Task Committee on Industrial Wastes in Cincinnati, January 23-24. The committee, which was organized last May, represents 22 major industrial groups of the country, in addition to state and federal public health interests. The chairman is Lyman Cox, supervisor, Engineering Service Division, E. I. DuPont de Nemours and Company, Wilmington, Del. The vice chairman is Dr. Harry Gehm, technical director of the National Council on Stream Improvement for the Pulp, Paper and Paperboard Industry, New York. Louis F. Warrick, chief, Technical Services Branch, Division of Water Pollution Control, Public Health Service, is secretary of the committee.

On the agenda for the meeting is a detailed inspection of the Environmental Health Center of the Public Health Service at Cincinnati. The work of the center, partcularly its industrial waste and water pollution projects, will be described by Vernon G. MacKenzie, officer in charge. Carl Schwob, chief of the Water Pollution Control Division, Public Health Service, will report to the committee on the progress of studies made in cooperation with the states under the Water Pollution Control Act of 1948. Scheduled reports from task groups are as follows: food industries, by Frank McKee, Kraft Foods Company, Chicago; mineral products, by L. C. Burroughs, Shell Oil Company, New York, and chemical processing, by Dr. Gehm. The meeting in Cincinnati will be the second convening of the committee since its establishment.

MEDICAL NEWS

COLORADO

Dr. Corper to Retire.—The National Jewish Hospital, Denver, announces the forthcoming retirement of Dr. Harry J. Corper, who for the past 30 years has been director of research. The research department of the hospital during this 30 year period has published many original investigations in the field of tuberculosis and has received numerous scientific awards, including the award from the Committee of Scientific Research of the American Medical Association, the Trudeau Medal of the National Tuberculosis Association, the Burdick Medal of the American Association of Clinical Pathologists and the Kober Medal of the American Association of Physicians. In recognition of the position that has been attained, the Board of Directors of the National Jewish Hospital propose to enlarge the facilities devoted to research. Plans are being developed for further recognition of Dr. Corper's outstanding services.

FLORIDA

Bust of Carlos Finlay.—The Cuban Government presented a bronze bust of Dr. Carlos Finlay to the University of Tampa December 3. The presentation was made by a delegation from Havana including Dr. Carlos M. Ramirez Corria, neurosurgeon, professor of the University of Havana and former secretary of the Cuban Health Service; Dr. Arturo Alfonso Rosello, past president of the Havana Lions Club; Armando Maribona, Havana journalist; and Domingo Ravenet, sculptor of the bust. Dr. Finlay a native of Camaguey, Cuba, received his medical education in the United States. He announced to the American Academy of Medical Sciences Aug. 14, 1881 that the mosquito was the carrier of yellow fever. His bust was sent to the university to commemorate past alliances in progress between Cuba and the United States and to symbolize future mutual advancement of cultural and trade relations between the two countries.

ILLINOIS

Report of Centennial Celebration.—The Adams County Medical Society's public celebration, "A Century of Health Progress," is reported to have been a success in every way except financially. None of the participants except the directing company of the pageant received any fees for participation. Members will be assessed to cover the deficit. An estimated 60,000 persons attended the free educational motion picture theater, and over 4,500 examinations comprising chest and dental roentgenograms, blood pressure determinations, hearing and sight tests were made. More than 10,000 persons attended the pageant, which had a cast of 450. Except for the pageant the celebration was free to the public.

Chicago

Illinois University Appointments.—The University of Illinois College of Medicine has announced the following faculty appointments: Oren C. Durham, Ph.D., has been named lecturer in allergy, with the rank of assistant professor. He has held the position of chief botanist at Abbott Laboratories since 1925. Dr. Daniel J. Pachman has been appointed clinical professor of pediatrics. Dr. Pachman has taught at Duke University School of Medicine, the University of Chicago School of Medicine and at Northwestern University Medical School. Dr. Edward Press has been appointed assistant professor of preventive medicine. He presently holds a full time appointment as associate director of the University of Illinois Division of Services for Crippled Children.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.

Chest Diseases in Industry.—The Chicago Tuberculosis Society and the Illinois Chapter of the American College of Chest Physicians will meet jointly January 12 at the Congress Hotel at 8: 00 p. m. Dr. Edward C. Holmblad will be moderator for a panel discussion on "Chest Diseases in Industry." Other participants include Drs. Joseph H. Chivers, Lloyd E. Hamlin, Jerome R. Head, David B. Radner and Thomas C. Angerstein, LL.B. The following cases will be presented: pulmonary effects of toxic fumes; case of combined siderosis, silicosis and tuberculosis; differential diagnosis of siderosis and silicosis; relation of trauma to pulmonary tuberculosis, and compensation problems in tuberculosis and in the pneumonoconioses. All physicians are invited. Dinner will be at 6: 30 p. m.

Course for Stutterers.—Northwestern University is preparing to institute a special evening course on its Chicago campus for adult stutterers. Instruction will be given every Tuesday from 6: 20 to 8: 00 p. m. for 18 weeks beginning February 5. Classes will be held in the Montgomery Ward Building at 301-303 East Chicago Avenue. Registration will be held from January 27 through February 3 on the fifth floor of Wieboldt Hall, 339 East Chicago Ave. The class will include lectures on the causes and nature of stuttering, discussions of problems faced by stutterers and their families and practical demonstrations of technics for controlling stuttering. The Northwestern University Speech and Hearing Clinic, one of the first of its type established in this country in 1926, has a staff of eight faculty members and 18 clinical workers. The clinic program is conducted in cooperation with Northwestern's Medical School and the School of Dentistry.

MASSACHUSETTS

Dr. Kellert Honored.—Dr. Ellis Kellert of Schenectady, N. Y., who this year terminated his long service as pathologist for Northern Berkshire's hospitals, was guest of honor at a dinner at the Williams Inn December 8 given by the trustees and medical and surgical staffs of both hospitals. He was presented appropriate gifts.

Postgraduate Course in Anesthesiology.—The Massachusetts Society of Anesthesiologists will present the third session of its annual postgraduate education course January 6 from 2: 30 to 5: 00 p. m. in Bigelow Amphitheater, Massachusetts General Hospital, Boston. Subjects to be discussed include pathology of the cardiovascular system and the psychological changes that would influence the conduct of anesthesia.

Dr. Stutzman Goes to Philadelphia.—Dr. Jacob W. Stutzman, associate professor of pharmacology at Boston University School of Medicine, has resigned to become director of the pharmacological laboratories at Smith, Kline and French Laboratories, in Philadelphia. Dr. Stutzman will continue to serve as special lecturer at the school. He was appointed to the faculty in 1947 and has conducted research on the pharmacology of anesthetic agents.

MICHIGAN

University Appointment.—Dr. Harper K. Hellems has been appointed assistant professor of medicine at Wayne University College of Medicine, Detroit. He has served on the staffs of the West Roxbury (Mass.) Veteran's Hospital and the Peter Bent Brigham Hospital in Boston.

Course in Radiological Health.—The School of Public Health of the University of Michigan, Ann Arbor, will conduct an inservice training course in radiologic health February 5-8, with the assistance of the Atomic Energy Commission, the Michigan Office of Civilian Defense and the U. S. Public Health Service. The course will provide public health workers with information that should aid in the understanding of some problems of civilian defense training. Content of the course

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includes orientation lectures, ways ionizing radiations are used, biological medical effects and public health implications. The enrolment fee is $5, which should be sent with applications for enrolment to H. E. Miller, School of Public Health.

MISSISSIPPI

Board Approves Student Loans.—The Mississippi State Medical Education Board in December approved 25 students for loans to become effective at midyear. Most of these students will enrol at the University of Mississippi School of Medicine, University, in January. State medical education loans are available to Mississippi citizens and residents for entering or completing medical education. The loan program was established by the 1946 legislature to help provide doctors especially in the rural areas of the state. Already 28 young physicians have entered practice in rural communities as a result of this plan, and over 35 young doctors now serving as interns will be ready to enter rural practice next summer. Announcement was made by the board that applications for loans to become effective in the summer and fall of 1951 may be received on and after March 1. The new deadline for receipt of all applications for summer and fall loans was set by the board as June 1, 1951. Deadline for receipt of all credentials for applications received prior to June 1 was set by the board as July 1, 1951.

NEW YORK

Auxiliaries Nursing Scholarships.—Doctors' wives in 22 New York counties are helping to overcome the shortage of nurses by providing 78 young women in the state with scholarships at present, according to a survey of the Woman's Auxiliary to the Medical Society of the State of New York. Nine nurses already have been graduated with this type of assistance.

New York City

Tumor Conference.—The January Tumor Conference of Harlem Hospital will be held January 24 at 11: 00 a. m. in the fifth floor Conference Room, Women's Pavilion. Dr. William L. Watson, attending surgeon on the thoracic and surgical service of Memorial Hospital, will speak on "Cancer of the Lung."

Dr. Curran Named Dean.—Dr. Jean A. Curran has been appointed dean of the State University College of Medicine in New York City. This is the first administrative appointment to the reorganized staff of the college, formerly the Long Island College of Medicine until its merger with State University of New York last April. Dr. Curran continues as chief administrative officer of the college, with which he has been associated since 1937, having served both as dean and president. Dr. Duncan W. Clark, who was dean of Long Island College of Medicine at the time of merger, has been appointed professor of environmental medicine and community health and executive officer of the newly constituted department.

Radiation Therapy Unit.—A powerful cancer-treating x-ray machine was dedicated at the Hospital for Joint Diseases December 3 in the new Lila Motley wing for radiation therapy. The machine and the building that contains it were built in honor of Lila Motley by her friends, the Federation of Jewish Philanthropies and other contributors. The machine is contained in a circular shaft 30 feet high and is housed in a vault built of concrete walls up to four feet thick. The building also contains two small x-ray units, the William Blau lecture hall and the School of Practical Nursing. The dedication program included addresses by Mrs. Martin Gross, president of the Lila Motley League; Dr. Maurice M. Pomeranz, director of the hospital's radiology service; Dr. Ross Golden, professor of radiology, Columbia University College of Physicians and Surgeons; Dr. Milton Friedman, attending radiation therapist at the hospital; Mr. Simon H. Fabian of the Federation of Jewish Philanthropies, and Dr. Charles S. Cameron, medical and scientific director of the American Cancer Society.

Personals.—A testimonial dinner was given on December 9 to Dr. John Duff on the completion of five years as president of the Medical Board of Morrisania City Hospital. The proceeds were contributed to the J. Lewis Amster Medical Library of the hospital. Dr. Amster, the toastmaster, introduced the following speakers: Dr. Marcus D. Kogel, commissioner of hospitals; Dr. Nathan B. Van Etten, former President of the American Medical Association; Dr. Jean A. Curran, dean of the State University College of Medicine in New York; Dr. Nathaniel Smith, medical superintendent, Morrisania City Hospital; Dr. John J. Roth, attending urologist, and Dr. John Duff, director of urology.——Dr. George W. Kosmak in September was given an honorary fellowship in the Royal College of Obstetricians and Gynecologists in England. Dr. Kosmak is editor of the *American Journal of Obstetrics and Gynecology* and the *New York State Journal of Medicine*. He has been a member of the board of directors of the Maternity Center Association for 31 years and chairman of its medical board for 19 years.——Dr. William A. Feirer, Philadelphia, has been appointed to the newly created post of vice president in charge of scientific affairs at E. R. Squibb & Sons, New York. For the past several years Dr. Feirer has been executive vice president of Sharp & Dohme.

NORTH CAROLINA

Orthopedic Clinic.—The new Wake County Orthopedic Clinic, established in the Wake County Health Department in Raleigh by the North Carolina League for Crippled Children, is for examination and discovery of orthopedic defects. No treatment will be given. Hours are the third Tuesday of each month at 9: 00 a. m.

Postgraduate Program.—The Raleigh Postgraduate Medical Program will extend from January 18 to March 1. Each speaker will deliver two papers, one at 4: 00 p. m. in the Nurses' Home, Rex Hospital, and the other at 8: 00 p. m. in the New Carolina Country Club. Lectures are as follows:

Jan. 18, Houston S. Everett, Baltimore, Early Diagnosis of Cancer in the Female Genital Tract; Methods of Treatment.
Jan. 25, Charles F. McKhann, Cleveland.
Feb. 1, Theodore R. Fetter, Philadelphia, Dysuria; Urinary Tract Infection.
Feb. 8, Julius Lempert, New York, Progress Made in Rehabilitation of the Deaf During the Last 15 Years.
Feb. 22, Alton Ochsner, New Orleans, La., Carcinoma of the Stomach; Acute Pancreatitis.
March 1, William Dameshek, Boston, Hypersplenism; Treatment of Anemia.

OHIO

Lecture on Amebiasis.—Dr. Harry Most, associate professor of preventive medicine, New York University College of Medicine, will address the staff of the Veterans Administration Hospital, Cleveland, on January 25 at 6:00 p. m. on "Amebiasis." All interested physicians are invited.

Premature Infants Program.—The Ohio Department of Health in cooperation with local health departments is helping to set up a referral system between hospitals and public health agencies whereby premature infants would be followed in the home by local public health nurses. The 1949 statistics on prematurity for the state are not available as yet. In 1949, however, 6.9 per cent of all newborn infants were born prematurely and 34.2 per cent of all infant deaths in the state were from prematurity.

OREGON

Home Safety Committee.—Dr. Harold M. Erickson, state health officer, has been appointed chairman of Governor Douglas McKay's home safety committee. Others elected are Dr. Harold E. Davis, representing the Oregon State Medical Society, vice president; George Sirino, superintendent of health and physical education for the state department of education, second vice president, and Thomas Leupp, Woodburn, representing public schools, secretary-treasurer. The committee has recommended adoption of a statewide building code for housing units embodying safety standards.

WASHINGTON

State Health Council.—Doctors, dentists, nurses and other professional health personnel have joined government and voluntary agencies to form a new State Health Council. Dr. Charles E. Watts, Seattle, president, said the objectives are to study present health problems, to make recommendation and, through joint action, to put findings into effect. Organizations that laid the foundation work for the council are the state dental, medical, hospital, pharmaceutical and nurses associations and the State Department of Health. Seven other health societies, the King County Central Blood Bank, professional schools of health sciences in the University of Washington and Washington State College and the Division of Vocational Rehabilitation of the State Board for Vocational Education are taking part in the council. Seymour Standish Jr., who has been doing health education work for the state department for the past four years, is the executive secretary. Offices are at 905 Second Avenue Building, Seattle.

WISCONSIN

Dr. Grove Made Professor Emeritus.—Announcement was made in November of the award of the title of professor emeritus to Dr. William E. Grove, former director of the division of otolaryngology of the Marquette University School of Medicine, Milwaukee. Dr. Grove has practiced in Milwaukee for more than 35 years. He was appointed to the Marquette medical school faculty in 1936 and six months later was named a clinical professor and director of the department of otclaryngology.

GENERAL

Institute on Oxygen Therapy.—This institute will be presented by the Inhalation Therapy Association of Chicago, a section of the Tri-State Hospital Assembly, at Alexian Brothers' Hospital, February 12-16. The institute will be sponsored by the Committee on Physiologic Therapy of the American College of Chest Physicians. This course is designed to instruct hospital personnel in the administration of inhalation therapy and will cover theory, treatment and bedside care. Application blanks may be secured from the Inhalation Therapy Association, 1230 East 63rd Street, Chicago 37. The registration fee is $25.

Meeting on Surgery of the Hand.—The sixth annual meeting of the American Society for Surgery of the Hand will be held January 26-27 at the Palmer House, Chicago, under the presidency of Dr. Condict W. Cutler Jr., New York. Invited speakers include:

H. Minor Nichols, Portland, Ore., Repair of the Extensor-Tendon Insertions in the Fingers.
Kenneth B. Jacques, Los Angeles, Cerebral Palsy as It Affects the Upper Extremities.
William Cooper, New York, Surgery of the Upper Extremity in Cerebral Palsy.
James G. Golseth, Pasadena, Calif., Electromyograms.
Don L. Eyler, Durham, N. C., and Charles E. Irwin, Warm Springs, Ga., Reconstructive Surgery on the Upper Extremity in Poliomyelitis.
Gordon H. Grant, Victoria, British Columbia, Methods of Treatment of the Hand and Dupuytren's Contracture.

Awards to the Fulbright Program.—The U. S. Department of State has announced that 14 awards have been allocated to the Fulbright program for the academic year 1951-1952 for university lecturing or advanced research "postdoctoral or equivalent" in Austria. Fields of activity include roentgen analysis of crystalline structures, anesthesia, ophthalmology, psychotherapy, surgery, radiology and radioisotopy. Among institutions to which awards may be tenable are Charles Francis University of Graz, Graz Institute of Technology, Leopold Francis University of Innsbruck; University of Vienna. The closing date for application is Jan. 15, 1951.

A number of foreign scholars have been awarded Fulbright travel grants for lecturing or advanced research in the fields of the natural sciences for the current academic year. These include 55 scholars in medicine. Information as to the names of the scholars, their actual or expected dates of arrival, the length of their time in the United States and the institutions which assume financial sponsorship of their visits may be obtained from the Conference Board of Associated Research Councils Committee on International Exchange of Persons, 2101 Constitution Avenue, Washington, 25.

Conference on Radiology.—The eighteenth annual Conference of Teachers of Clinical Radiology will be held at the Palmer House in Chicago, February 10. All radiologists are invited to attend. The subject of the conference is "Radiologic Defense." Speakers are as follows:

Norvin C. Kiefer, National Security Resources Board, Washington, D. C., Mobilization of Health Resources for Defense.
Brig. Gen. James P. Cooney, (USA, MC), Atomic Energy Commission, Washington, D. C., The Duties of Physicians in an Atomic Disaster.
Elbert DeCoursey, director, Armed Forces Institute of Pathology, Washington, D. C., Atomic Bomb Effects—Teaching Aids from Armed Forces Institute of Pathology.
Lieut. Comdr. Eugene Cronkite (USN, MC), Naval Medical Research Institute, Bethesda, Md., Diagnosis and Treatment of Radiation Injuries.
William F. Bale, Ph.D., Atomic Energy Commission, Rochester, N. Y., Training for the Detection of Radiation Hazards: Instruments; Personnel.
Claude R. Schwob, Ph.D., Naval Radiation Laboratory, San Francisco, Radioactive Decontamination.

Dr. Charles E. Virden, Kansas City, Mo., president of the American College of Radiology, will speak at the luncheon at 12:15 p. m. The conference is being sponsored by the American College of Radiology.

Academy of Allergy Meeting.—The seventh annual meeting of the American Academy of Allergy will be held February 5-7 at the Hotel Statler, New York. William F. Hamilton, Ph.D., professor of physiology, University of Georgia School of Medicine, Augusta, will speak on "The Physiology of Pulmonary Circulation." Pulmonary function studies in asthma will be discussed in papers to be presented by Dr. Daniel S. Lukas, director of the Cardio-Respiratory Function Laboratory at the New York Hospital, and by Dr. Henry D. Beale, Boston. Studies on the practical value and limitations of pulmonary function tests will be reported by a group from the Allergy Unit of the University of Illinois College of Medicine. David Pressman, Ph.D., Sloan-Kettering Institute for Cancer Research, will deliver an address. Papers dealing with antigens and antibodies labeled with iodine 131 will be presented by speakers from Washington University School of Medicine, St. Louis. The Wednesday session will comprise papers on cortisone and pituitary adrenocorticotropic hormone (ACTH). Dr. A. McGehee Harvey, professor of medicine and director of the department, Johns Hopkins University School of Medicine, will speak on "The Use of ACTH and Cortisone in Allergic Diseases." Immunologic, hematologic, metabolic and physiological effects and clinical studies of results of treatment with adrenal cortex hormones will be discussed.

International Study on ACTH and Cortisone.—Plans for an international cooperative study of the effectiveness of the hormone substance pituitary adrenocorticotropic hormone (ACTH) and cortisone in the treatment of rheumatic fever and the prevention of rheumatic heart disease were announced December 19 by the American Council on Rheumatic Fever of the American Heart Association. The long term study will be conducted through a central coordinating center in New York City and at 12 cooperating research centers in the United States, Canada and Great Britain. The council's Committee on Criteria and Standards, headed by Dr. David D. Rutstein, professor of preventive medicine, Harvard Medical School, Boston, will coordinate the investigation at the central office in New York. Under the study plan, patients treated during acute attacks of rheumatic fever during the next calendar year will be followed for at least three years. Investigators in the United States and Canada will report their findings to the New York coordinating center, where a continuous analysis will be made. These findings will be compared with results obtained by a special committee of the Medical Research Council in England, to which the British centers will report. Grants to help finance the study have been made by the National Heart Institute of the United States Public Health Service. Amounts totalling close to $200,000 will go to the coordinating center and principal investigators of cooperative research centers in New York, Boston, Denver and Chicago.

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In addition, the Armed Forces Epidemiological Board and the U. S. Air Force will finance a cooperating research center at the Francis E. Warren Air Force Base in Wyoming. A research center in Toronto, Ontario, is being financed by the Canadian Rheumatism and Arthritis Foundation. In England the individual research centers and the Medical Research Council are financing the studies there. Armour & Co., Chicago, which produces ACTH, and Merck & Co., Inc., Rahway, N. J., which produces cortisone, have contributed $5,000 each to pay for the planning of the study and will contribute the large amounts of ACTH and cortisone necessary for the study.

CORRECTION

Bite of Black Widow Spider.—The first word of the title of the abstract on this subject on page 1305 of THE JOURNAL of Dec. 9, 1950, should have been "Physostigmine," rather than "Neostigmine."

Artificial Respiration.—In the article on "Artificial Respiration: A New Method and a Comparative Study of Different Methods in Adults" in THE JOURNAL, Dec. 23, 1950, page 1458, the second and third lines of table 1 should have read: "Hip lift (Emerson)" and "Prone pressure (Schafer)."

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 26-28. Sec., Dr. D. G. Gill, 519 Dexter Ave., Montgomery.

ARIZONA: * *Examination.* Phoenix, Jan. 17-19. *Reciprocity.* Phoenix, Jan. 20. Sec., Dr. J. H. Patterson, 316 W. McDowell Road, Phoenix.

ARKANSAS: * *Regular.* Little Rock, June 7-8. Sec., Dr. Joe Verser, Harisburg. *Eclectic.* Little Rock, June 7-8. Sec., Dr. C. H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Written.* Los Angeles, Feb. 26-March 1. *Oral.* San Francisco, Jan. 20. Los Angeles, Feb. 24. *Oral and Clinical for Foreign Medical School Graduates.* Los Angeles, Feb. 25. Sec., Dr. Frederick N. Scatena, 1020 N St., Sacramento 14.

CONNECTICUT: * *Examination.* Hartford, March 13-14. Sec. to the Board, Dr. Creighton Barker, 160 St. Ronan St., New Haven. *Homeopathic.* Derby, March 13-14. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

DELAWARE: Dover, Jan. 9-11. *Reciprocity.* Jan. 18, 1951. Sec., Dr. J. S. McDaniel, 229 S. State St., Dover.

GEORGIA: Atlanta, June. Augusta, June. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. John Y. Battenfield, Agana.

HAWAII: Honolulu, Jan. 8-11, 1951. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

IDAHO: Boise, Jan. 8, 1951. Sec., Mr. Armand L. Bird, 305 Sun Bldg., Boise.

ILLINOIS: Chicago, Jan. 9-11. Superintendent of Registration, Mr. Charles F. Kervin, Capitol Bldg., Springfield.

INDIANA: Indianapolis, June 20-22. Exec. Sec., Miss Ruth V. Kirk, 1138 K. of P. Bldg., Indianapolis 4.

IOWA: * *Written.* Iowa City, June 11-13. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

MAINE: Portland, March 12-13. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: Baltimore, June 19-22. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 1.

MASSACHUSETTS: Boston, Jan. 23-26, 1951. Sec., Dr. Geo. R. Schadt, 37 State House, Boston.

MINNESOTA: * Minneapolis, Jan. 16-18. Sec., Dr. J. F. Du Bois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSOURI: *Examination.* Jefferson City, Feb. 19-21. *Reciprocity.* Jefferson City, Feb. 12. Ex. Sec., Mr. John A. Hailey, Box 4, Jefferson City.

MONTANA: Helena, April 2-4. Sec., Dr. S. A. Cooney, 214 Power Block, Helena.

NEBRASKA: * June 1951. Director, Mr. Oscar F. Humble, Room 1009, State Capitol Bldg., Lincoln.

NEVADA: Carson City, Feb. 5. Sec., Dr. George H. Ross, 112 Curry St., Carson City.

NEW HAMPSHIRE: *Examination.* Concord, March 14-15. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 19-22. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, April 10-11. Sec., Dr. Charles J. McGoey, Coronado Bldg., Santa Fe.

NEW YORK: *Examination.* Albany, Buffalo, Syracuse and New York City, Jan. 30-Feb. 2. Sec., Dr. Jacob L. Lochner, 23 S. Pearl St., Albany.

NORTH CAROLINA: *Reciprocity.* Winston-Salem, Jan. 15. Sec., Dr. Joseph J. Combs, 419 Professional Bldg., Raleigh.

OKLAHOMA: * *Examination.* Oklahoma City, June 6-7. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

PENNSYLVANIA: Philadelphia, January 1951. Acting Secretary, Mrs. M. G. Steiner, 351 Education Bldg., Harrisburg.

PUERTO RICO: *Examination.* Santurce, March 6. Sec., Mr. Luis Cueto Coll, Box 3717, Santurce.

SOUTH CAROLINA: *Reciprocity.* Columbia, Feb. 6, March 5, April 2. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA: * Jan. 15-16. Sioux Falls, South Dakota. Sec., Dr. C. E. Sherwood, 109 Center St., West, Madison.

UTAH: Salt Lake City, July 1951. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

VERMONT: Burlington, February 1951. Sec., Dr. F. J. Lawliss, Richford.

VIRGIN ISLANDS: St. Thomas, June 12. Sec., Dr. Earle M. Rice, St. Thomas.

WASHINGTON: * Seattle, January 1951. Sec., Mr. Edward C. Dohm, Department of Licenses, Olympia.

WEST VIRGINIA: Charleston, Jan. 8-10. Sec., Dr. N. H. Dyer, State Capitol, Charleston 5.

WISCONSIN: * River Falls, Jan. 9-11, 1951. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls.

WYOMING: *Examination.* Cheyenne, Feb. 5. Sec., Dr. Franklin D. Yoder, Capitol Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

CONNECTICUT: *Examination.* Feb. 10. Executive Asst., State Board of Healing Arts, Mr. M. G. Reynolds, 110 Whitney Ave., New Haven 10.

DISTRICT OF COLUMBIA: *Examination.* April, 1951. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.

FLORIDA: *Examination.* Gainesville, June 2. Sec., Mr. M. W. Emmel, University of Florida, Gainesville.

IOWA: *Examination.* Des Moines, Jan. 9. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.

MICHIGAN: *Examination.* Detroit and Ann Arbor, Jan. 12-13. Sec., Miss Eloise LeBeau, 101 No. Walnut St., Lansing 15.

NEBRASKA: *Examination.* Omaha, Jan. 9-10. Dir., Mr. Oscar F. Humble, Room 1009, State Capitol Bldg., Lincoln 9.

OKLAHOMA: *Examination.* Oklahoma City, March 27. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

RHODE ISLAND: *Examination.* Providence, Feb. 14. Chief, Division of Professional Regulation, 366 State Office Bldg., Providence.

TEXAS: *Examination.* Latter Part of April. Sec., Bro. Raphael Wilson, 306 Nalle Bldg., Austin.

WASHINGTON: Seattle, January 1951. Sec., Mr. Edward D. Dohm, Department of Licenses, Olympia.

WISCONSIN: *Examination.* Madison, April 7. Sec., Mr. W. H. Barber, Scott and Watson Sts., Ripon.

* Basic Science Certificate required.

MEETINGS

ANNUAL CONGRESS ON INDUSTRIAL HEALTH, Atlanta Biltmore Hotel, Atlanta, Ga., Feb. 26-28. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago 10, Secretary.

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE, Palmer House, Chicago, Feb. 12-13. Dr. Donald G. Anderson, 535 N. Dearborn St., Chicago 10, Secretary.

NATIONAL CONFERENCE ON RURAL HEALTH, Peabody Hotel, Memphis, Tenn., Feb. 23-24. Dr. F. S. Crockett, 535 N. Dearborn St., Chicago 10, Chairman.

AMERICAN ACADEMY OF ALLERGY, Hotel Statler, New York, Feb. 5-7. Dr. Walter S. Burrage, 208 E. Wisconsin Ave., Milwaukee 2, Secretary.

AMERICAN ACADEMY OF FORENSIC SCIENCES, Chicago, Drake Hotel, March 1-3. Prof. Ralph F. Turner, Michigan State College Dept. of Police Administration, East Lansing, Mich., Secretary.

AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS, Palmer House, Chicago, Jan. 27-Feb. 1. Dr. Harold B. Boyd, 122 S. Michigan Ave., Chicago 3, Secretary.

AMERICAN SOCIETY FOR SURGERY OF THE HAND, Palmer House, Chicago, Jan. 26. Dr. Joseph H. Boyes, 1401 S. Hope St., Los Angeles 15, Secretary.

ATLANTA GRADUATE MEDICAL ASSEMBLY, Municipal Auditorium, Atlanta, Ga., Feb. 5-7. Mrs. Stewart R. Roberts, 768 Juniper St. N.E., Atlanta, Executive Secretary.

CENTRAL SURGICAL ASSOCIATION, Chicago, Feb. 22-24. Dr. James T. Priestley, Mayo Clinic, Rochester, Minn., Secretary.

INTERNATIONAL POST-GRADUATE MEDICAL ASSEMBLY OF SOUTHWEST TEXAS, Municipal Auditorium, San Antonio, Jan. 23-25. Dr. John H. Hinchey, P. O. Box 2445, San Antonio 6, Secretary.

MIDDLE ATLANTIC STATES REGIONAL CONFERENCE, Philadelphia, Jan. 18. Dr. William Bates, 2029 Pine St., Philadelphia 3, Secretary.

NATIONAL CONFERENCE ON MEDICAL SERVICE, Palmer House, Chicago, Feb. 11. Dr. R. E. Fitzgerald, 2218 N. Third St., Milwaukee 12, Secretary.

SECTIONAL MEETING, AMERICAN COLLEGE OF SURGEONS, Hotel Statler, St. Louis, Jan. 22-23. Dr. James Barrett Brown, 508 N. Grand Blvd., St. Louis, Chairman.

SOUTH CENTRAL BRANCH, AMERICAN UROLOGICAL ASSOCIATION, Hotel Adolphus, Dallas, Jan. 29-Feb. 2. Dr. Rex E. Van Duzen, 721 Medical Arts Bldg., Dallas, Chairman.

DEATHS

Mariette, Ernest Sidney, Wayzata, Minn.; born in Good Thunder, Minn., Jan. 3, 1888; University of Minnesota Medical School, Minneapolis, 1913; specialist certified by the American Board of Internal Medicine; clinical assistant professor of medicine at his alma mater and the University of Minnesota Graduate School; fellow of the American College of Physicians and the American College of Hospital Administrators; member of the American Medical Association and the American Trudeau Society; formerly member of the board of directors of the National Tuberculosis Association and on various councils and committees of the American Hospital Association; served as secretary of the Hennepin County Commission on Tuberculosis, as president of the Minnesota Trudeau Society, Hennepin County Tuberculosis Association, Minnesota Sanatorium Association, Minnesota Hospital Association, Mississippi Valley Conference on Tuberculosis and the Mississippi Valley Trudeau Society; formerly medical director and superintendent of the Glen Lake Sanatorium in Oak Terrace; died in Eitel Hospital, Minneapolis, October 29, aged 62, of hypertensive cardiovascular disease with cerebral thrombosis.

King, Walter Wood ✙ Medical Director, U. S. Public Health Service, retired, Washington, D. C.; born Dec. 18, 1875; University of Louisville (Ky.) Medical Department, 1897; entered the public health service on March 13, 1899; from 1902 to 1906 chief quarantine officer of Puerto Rico; sent on many quarantine and sanitary inspection tours in this country and abroad, including Italy, England, Turkey and France; at the time of his retirement in January 1933 was medical officer of the Coast Guard; in 1925 was an American delegate to the first International Congress on Malaria in Rome; died in the U. S. Marine Hospital, Baltimore, October 9, aged 74, of encephalomalacia, cerebral and coronary arteriosclerosis with infarction.

McFarland, William West ✙ Berkeley Springs, W. Va.; born in Alleghany, Pa., Dec. 10, 1878; University of Pennsylvania Department of Medicine, Philadelphia, 1902; member of the Medical Society of the State of Pennsylvania and the American Public Health Association; formerly practiced in Pittsburgh, where he was vice president of the Pittsburgh Academy of Medicine, director of health, medical supervisor in the city bureau of child welfare, member of the school medical inspection staff and affiliated with St. Francis Hospital; past president of the Pennsylvania Public Health Association; died October 14, aged 71, of coronary thrombosis.

McFarland, Warren Chamberlain, Warwick, N. Y.; Yale University School of Medicine, New Haven, Conn., 1887; formerly professor of otolaryngology at New York Post Graduate Medical School and Hospital, Columbia University, New York; member of the American Medical Association, past president of the New York Otological Society; served on the staffs of the Elizabeth A. Horton Memorial Hospital in Middletown, Bronx, and the Manhattan Eye, Ear and Throat hospitals in New York; died October 18, aged 84, of tuberculosis of the skin, arteriosclerosis and chronic myocarditis.

Donaldson, Joel Singleton, Oakland, Miss.; Memphis (Tenn.) Hospital Medical College, 1901; member of the American Medical Association; died October 25, aged 83, of carcinoma of the prostate.

Fay, Emma Hooker, Northboro, Mass.; Boston University School of Medicine, 1909; member of the New England Society of Psychiatry; for many years affiliated with the Westboro (Mass.) State Hospital; died October 22, aged 86.

Fee, Louis Walter, Pueblo, Colo.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; died November 7, aged 74, of cerebral hemorrhage.

✙ Indicates Fellow of the American Medical Association.

French, Elmo Dial ✙ Miami, Fla.; University of Texas School of Medicine, Galveston, 1916; member of the American Academy of Dermatology and Syphilology; specialist certified by the American Board of Dermatology and Syphilology; affiliated with Jackson Memorial Hospital; died October 24, aged 60, of coronary occlusion.

Gillespie, Paul Bernard, Santa Ana, Calif.; John A. Creighton Medical College, Omaha, 1917; member of the American Medical Association; died October 22, aged 61, of pancreatitis.

Gregor, Oscar, Schenectady, N. Y.; Universita Karlova Fakulta Lékařská, Praha, Czechoslovakia, 1926; member of the American Medical Association; specialist certified by the American Board of Ophthalmology; formerly assistant in ophthalmology at the New York University College of Medicine; on the staff of Ellis Hospital, where he died October 23, aged 48.

Hammer, William James, New York; Cornell University Medical College, New York, 1902; served during World War I; formerly medical director of the New York Life Insurance Company; died in the New York Hospital, October 13, aged 71.

Hartwell, Robert William, Beaumont, Calif.; Cooper Medical College, San Francisco, 1911; served during the Spanish-American War and World War I; died in Loma Linda Sanitarium and Hospital in Loma Linda, October 9, aged 75, of cerebral hemorrhage.

Hobson, Arthur Bronson, Salem, Ohio; University of Wooster Medical Department, Cleveland, 1895; died October 26, aged 79.

Holbrook, William Henry, Atlanta, Ga.; Atlanta Medical College, 1898, died in Pickens, S. C., October 8, aged 75, of injuries received in an automobile accident.

Holt, Edward Wells Atwood, North Andover, Mass.; Harvard Medical School, Boston, 1903; member of the American Medical Association; died October 28, aged 71, of coronary thrombosis.

Hurst, Jonas Levi, Dorset, Ohio; Eclectic Medical Institute, Cincinnati, 1902; member of the American Medical Association; for many years member of the board of education and county health commissioner; died October 30, aged 72, of coronary thrombosis.

Jones, Archie ✙ Newberry, Mich.; the Hahnemann Medical College and Hospital, Chicago, 1920; affiliated with Newberry State Hospital, where he died October 5, aged 60.

Keating, David Mitchell, Cleveland; St. Louis University School of Medicine, 1926; member of the American Medical Association; formerly vice president of the Academy of Medicine of Cleveland; associated with St. Luke's Hospital; served during World War I; died in University Heights, Ohio, October 18, aged 52, of carcinoma of the colon.

Klein, Hilbert Philmon, Fort Branch, Ind.; Eclectic Medical Institute, Cincinnati, 1897; member of the American Medical Association; died October 31, aged 76.

Laux, Leo John, Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1917; member of the American Medical Association; served during War I; formerly practiced in Sayre, Pa., where he was affiliated with Robert Packer Hospital and was on the school board; for many years associated with the Veterans Administration; died October 23, aged 55.

MacCrowe, Albert Edward Charles, Baltimore; Baltimore Medical College, 1904; died in New York October 29, aged 71, of heart disease.

McDonnell, Clarence H., ✙ Sacramento, Calif.; Barnes Medical College, St. Louis, 1909; retired county autopsy surgeon; on the staff of Mercy Hospital, where he died October 22, aged 71, of coronary sclerosis and mitral stenosis.

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McHugh, John Francis ⊕ Shelby, Ohio; University of Louisville (Ky.) Medical Department, 1921; president of the staff of Shelby Hospital; died in City Hospital, Worcester, Mass., October 24, aged 53, of injuries received in an automobile accident.

McKelvey, Robert Harrison, Salem, Ohio; Ohio State University College of Medicine, Columbus, 1933; member of the American Medical Association; served during World War II; affiliated with Salem City Hospital; died November 1, aged 45.

McKnight, George Scott, Avon Park, Fla.; University of Pennsylvania Department of Medicine, Philadelphia, 1904; past president of De Soto-Hardee-Highland-Charlotte-Glades Counties Medical Society; member of the city council and city health officer; died October 10, aged 72, of angina pectoris.

Meltzer, Victor John ⊕ New York; College of Physicians and Surgeons of Chicago, 1895; died recently, aged 79.

Nichols, Robert Henry, Watertown, Mass.; Middlesex College of Medicine and Surgery, Cambridge, Mass., 1927; member of the American Medical Association; died recently, aged 73, of carcinoma of the rectum.

Perkins, Frederick Payne ⊕ Scottsdale, Ariz.; Louisville (Ky.) Medical College, 1906; served with the Arizona National Guard during World War II; formerly secretary and state superintendent of public health of Arizona; for many years director of health at the University of Arizona in Tucson; affiliated with the Veterans Administration Regional Office in Phoenix; died in the Veterans Administration Hospital, Phoenix, October 29, aged 69, of acute myocardial infarction.

Peters, Isaac Taylor, Princeton, W. Va.; Medical College of Virginia, Richmond, 1918; member of the American Medical Association; past president of the McDowell County Board of Education; died in Huntington October 7, aged 60, of arteriosclerosis.

Pollock, Milton De Witt ⊕ Decatur, Ill.; Rush Medical College, Chicago, 1895; an Associate Fellow of the American Medical Association; member of the American Association of Railway Surgeons; affiliated with St. Mary's Hospital, Decatur and Macon County Hospital and Wabash Employes' hospitals; died in the Illinois State Hospital, Jacksonville, October 18, aged 87, of myocarditis.

Poynter, Charles William McCorkle, Omaha; University of Nebraska College of Medicine, Omaha, 1902; dean emeritus and professor of anatomy emeritus at his alma mater; member of the American Association of Anatomists and the American Medical Association; died October 25, aged 75, of leukemia.

Premer, James Frederick ⊕ Benkelman, Neb.; University of Nebraska College of Medicine, Omaha, 1908; past president of the Southwest Nebraska Medical Association; died recently, aged 69.

Pusey, Charles Meigs, Oakland, Calif.; University of Louisville (Ky.) Medical Department, 1884; for many years surgeon of the Illinois-Central Railroad; died October 14, aged 90, of myocardial infarction.

Rauth, Emil, Brooklyn; College of Physicians and Surgeons, medical department of Columbia College, New York, 1886; member of the American Medical Association; died November 12, aged 89, of cerebral hemorrhage.

Retts, John P., Martinsville, Ind.; Medical College of Indiana, Indianapolis, 1901; died recently, aged 80.

Richardson, R. C., Pheba, Miss.; Memphis (Tenn.) Hospital Medical College, 1901; died November 15, aged 74.

Robinson, Harrison Leonard, Bangor, Maine; Medical School of Maine, Portland, 1914; served during World War I; member of the New England Surgical Society; for two terms served on the city council; affiliated with Eastern Maine General Hospital and Stinson Private Hospital; died October 24, aged 61, of cirrhosis of the liver.

Rowe, Anderson Mazetta, Bowling Green, Ky.; Hospital College of Medicine, Louisville, 1898; died October 2, aged 86.

Ryan, Maria Page, Atlantic City, N. J.; Woman's Medical College of Pennsylvania, Philadelphia, 1911; died October 31, aged 87.

Schwarz, Wolf Samuel, New York; Medizinische Fakultät der Universität, Wien, Austria, 1929; died October 2, aged 57.

Sharpe, Charles Tilley ⊕ New York; Manitoba Medical College, Winnipeg, Man., Canada, 1898; member of the Radiological Society of North America; died in St. Luke's Hospital October 27, aged 75, of coronary thrombosis.

Short, John Wesley, Constantia, N. Y.; Syracuse University College of Medicine, 1903; died in St. Michaels, Md., October 15, aged 70, of coronary thrombosis.

Smith, Robert Holbrook ⊕ Akron, Ohio; Rush Medical College, Chicago, 1910; co-founder of Alcoholics Anonymous; on the staff of St. Thomas Hospital and City Hospital, where he died November 16, aged 71.

Smith, William Adams, Batavia, N. Y.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1905; at one time professor of pathology and bacteriology at the West Virginia University School of Medicine in Morgantown; served on the staffs of various Veterans Administration hospitals; died November 12, aged 69, of arteriosclerosis and uremia.

Snead, Henry Martin, Columbia, Va.; University College of Medicine, Richmond, 1907; head of the Petersburg Draft Examining Board during World War II; member of the American Medical Association; past president of the Petersburg Medical Faculty; served as coroner of the city of Petersburg and health officer of Amelia, Goochland, Powhatan, Loudoun, Louisa and Fluvanna counties; died October 8, aged 65, of carcinoma of the pancreas.

Spitaleri, Leonard Joseph, New York; Fordham University School of Medicine, New York, 1921; member of the American Society of Anesthesiologists and the American Medical Association; died in Greenwood Lake, N. Y., November 4, aged 53.

Stevens, Thomas H., San Diego; Baltimore Medical College, 1893; died October 17, aged 89, of carcinoma of the colon.

Stewart-Perley, Melba D., ⊕ Laconia, N. H.; University of Pittsburgh School of Medicine, 1926; specialist certified by the American Board of Radiology; member of the New England Roentgen Society and Radiological Society of North America; died in Chicago October 27, aged 49, of chronic myocarditis.

Stone, John Thomas, Glen Burnie, Md.; Duke University School of Medicine, Durham, N. C., 1942; served during World War II; formerly a resident physician at the Presbyterian Hospital in New York, Veterans Administration Hospital in Richmond, Va., and St. Francis Hospital in Wilmington, Del.; died in Baltimore, October 24, aged 33.

Tatum, Samuel Carter, Centre, Ala.; Vanderbilt University School of Medicine, Nashville, Tenn., 1893; member of the American Medical Association; county health officer; killed in an automobile accident October 22, aged 79.

Tilock, Walter William, Lorain, Ohio; Eclectic Medical College, Cincinnati, 1926; member of the American Medical Association; on the staff of St. Joseph's Hospital; died October 14, aged 55, of coronary heart disease.

Vallotton, Joseph Ralph ⊕ Daytona Beach, Fla.; University of Georgia School of Medicine, Augusta, 1934; member of the American Association of Industrial Physicians and Surgeons; member of the state board of medical examiners; served as a lieutenant commander in the U. S. Naval Reserve during World War II; member of the surgical staff of the Halifax District Hospital; died October 5, aged 41, of acute coronary occlusion.

Williams, David Rowland, Girard, Ohio; Columbus Medical College, 1891; member of the American Medical Association; for many years served on the board of education and as public health officer of Liberty Township; on the adjunct staff of the North Side Unit of Youngstown (Ohio) Hospital, where he died October 15, aged 87, of fracture of the fourth vertebra and cerebral edema.

FOREIGN LETTERS

LONDON Oct. 27, 1950.

Nutrition and Antibodies.—In a leading article, the *Lancet* reviews some recent investigations on the relation of nutrition to antibody production. It is true, they say, that Gell in 1948 found that well nourished British soldiers had better antibody responses than half-starved German civilians, but, he remarked, the differences were slight. Balch (*J. Immunol.* **64**:397 [May] 1950) now measures the diphtheria antitoxin production of two groups of patients whose nutritional states differed widely.

One group consisted of 25 severely ill patients, many with advanced malignant disease and most with a low serum protein level, who had lost up to 40 per cent of their normal body weight. In other words, they were comparable to emaciated victims of Belsen.

The other group contained 19 well nourished subjects, of whom five were in good health, six had inguinal hernias and eight had either cerebral vascular accidents or cardiovascular disease without cardiac failure. All had maintained normal weight for at least six months.

The investigator chose diphtheria antitoxin as the test antibody because (1) the antigen, diphtheria toxoid, can be obtained in a highly purified form, (2) in immune persons the antitoxin response is high and relatively uniform and can be accurately estimated even in low concentration and (3) with purified toxoid the antitoxin is the only antibody produced, so that its concentration in the serum is a measure of the patient's total capacity to produce circulating antibody. All patients of the two groups were first proved to be Schick-negative, and each then was given intramuscularly 0.12 mg. of toxoid. Thereafter blood antitoxin levels were ascertained at three day intervals for at least three weeks and in some patients at longer intervals, until death. A rise in the circulating antitoxin was usually noted within four days of the toxoid injection, with a maximum response between the fourteenth and twenty-fourth days. The amount of antibody produced varied greatly between one patient and another, but there was no indication that in the depleted group the response depended on age, on serum protein, serum albumin or serum globulin levels or, surprisingly, on the antibody level before the test dose of the antigen was given. A number of patients showing the poorest antibody response did not acquire infection, whereas in others infections developed although their antibody production was normal.

Balch concedes that his results do not show whether diets rich in protein may enhance antibody production, and he doubts whether antibody production is of prime importance in postoperative infections. Wound sepsis, hypostatic pneumonia, peritonitis and genitourinary infections are more probably caused by interference with the circulation than by failure of the organism to produce antibodies. Balch thinks that the relation between nutrition and antibody production may be more subtle than has been suggested by Cannon, who holds that protein depletion means failure of antibody production and that this failure can be corrected by protein repletion. For example, Stoerk and co-workers showed that pyridoxine-deficient rats produced less antibody to sheep erythrocytes than rats given a complete diet (normal controls) or a diet reduced in quantity to equal that eaten by the pyridoxine-deficient animals (inanition controls). A similar observation has been reported by Axelrod and co-workers and by Agnew and Cooke with sheep erythrocytes and typhoid H antigen. Like Balch, Stoerk and others and Agnew and Cook observed that the inanition controls tended to produce more antibody than the normal controls. Pyridoxine deficiency interferes with amino acid metabolism and may thus hinder globulin synthesis, and Stoerk and co-workers suggest that this may impair antibody production perhaps directly by causing lymphoid atrophy, which is a feature of pyridoxine deficiency. The importance of the lymphocyte in antibody production is now well established. The article concludes with the statement that it would seem that reduction of the dietary protein is less likely to hinder antibody production than is interference with protein metabolism.

Prolonged Intercostal Paralysis Due to a Relaxant.—In a recent issue of the *British Medical Journal* the attention of anesthetists is called to a potential complication arising from the use of the relaxant flaxedil® (1,2,3-tri[diethylaminoethoxy] benzene triethyliodide) in patients with diminished kidney function. H. B. Fairley, M.B., of the Department of Anesthetics, Westminster Hospital, reports a case of prolonged intercostal paralysis following the intravenous administration of 140 mg. of flaxedil® to a woman with severe renal damage. The author suggests that the prolonged action of the drug might be due to its delayed excretion in the urine.

His patient, aged 33, had a history of chronic nephritis for seven years with attacks of blurred vision for two years. She was hospitalized for hysterotomy and sterilization. At the time of operation she appeared well but had ankle edema, albuminuria, hypertension (blood pressure 180/110) and anemia (hemoglobin 55 per cent). Her blood urea level was 60 mg. per 100 cc., and her urea clearance test showed pronounced impairment of renal function. Anesthesia was induced with 0.4 Gm. of thiopental sodium and continued, after intubation, with a mixture of nitrous oxide, oxygen and minimal cyclopropane. Initial intravenous administration of 100 mg. of flaxedil® was followed, 30 minutes later, by a dose of 40 mg., because of tightening of the abdominal muscles. After each dose, respirations returned in about two minutes. Assisted respiration was continued throughout, since the patient was in the Trendelenburg position. The operation was completed in 55 minutes. Postoperatively respirations remained shallow and purely diaphragmatic for 13 hours, and it was necessary to employ intubation, suction and oxygen to prevent cyanosis. During this time the clinical picture was complicated by symptoms suggestive of hypertensive encephalopathy. Shortly after the administration of 0.43 mg. of atropine and 1.25 mg. of neostigmine, intercostal respirations were resumed and the patient's condition returned to normal.

PARIS Aug. 20, 1950.

Treatment of Nephropathies with Testosterone Propionate.—In Prof. Justin Besancon's ward at the Bichat Hospital, H. P. Klotz and J. Debray used testosterone propionate, with remarkable results, in a 38 year old patient whose three year stay in a concentration camp had initiated a polyendocrine syndrome, predominantly hypoandrogenic, and chronic asymptomatic nephritis, with azotemia cylindruria, and impairment of renal function. Excretion of 17-ketosteroids was only 3.9 mg.; urinary estrogen and gonadotropin were almost normal. Implantation of three pellets of 100 mg. of testosterone propionate produced, in addition to the expected effect on sexual potency, hirsutism, spasmophilia and improvement in renal function lasting five months. A second implantation again improved the renal syndrome; this has lasted 15 months, with only a deficiency in glomerular clearance remaining. A 17 year old patient with a severe renal deficiency and infantilism was also greatly improved by injections of microcrystals of testosterone propionate. Besancon, Klotz and Cournot, encouraged by these results, have used the drug in 11 new cases,

The items in these letters are contributed by regular correspondents in the various foreign countries.

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with beneficial results in four. In a menopausal patient with azotemia (0.95 Gm.) and slight renal deficiency, the daily injection of 45 mg. of testosterone propionate in oil for 45 days caused the blood urea to fall, while an implant of 400 mg. of testosterone propionate maintained the urea rate at 0.30 Gm. and improved renal function. After four months a relapse necessitated another implantation. In a female diabetic with azotemia (1-1.35 Gm. per liter) and serious renal disorders, implantation of 600 mg. caused the urea to fall to 0.30-0.40 Gm. and improved renal function for seven months; a second implantation was ineffective. In a patient with azotemia (0.68-0.86 Gm.) 24 injections of testosterone propionate (25 mg. every second day) caused a fall to 0.31 Gm. In a patient with lead intoxication with renal insufficiency, injection of microcrystals of testosterone propionate caused the urea level and renal function to return to normal. The authors record failures in three cases of azotemic and hypertensive nephritis and in one case each of albuminuria, chronic nephritis, malignant nephroangiosclerosis and hematuric nephritis. Testosterone therapy appears to be indicated in renal disorders associated with certain types of hypogonadism. Untoward reactions include edema, in two cases, accompanied with an increase in weight (not similar to the increase of weight often observed after the implantation of testosterone), rise in blood pressure and decrease of diuresis. More rarely, fluxions in the knee joint as described by Guy Laroche and Perrault were noted. These disappear within a few days. The authors advise that this treatment not be used in the presence of peripheral or pulmonary edema.

ANURIC NEPHRITIS

Derot and Bernier tried testosterone propionate in toxic or infectious anuric nephritis after having noted that elimination of 17-ketosteroids was normal or lowered while that of 11-oxysteroids was considerably increased. This imbalance of adrenal hormones explains, in part, the excess production of uric acid and urea. In four cases of anuria due to Clostridium perfringens and lead poisoning, they noted the slowness of the azotemic rise each time testosterone proprionate was administered. In two cases of polycystic kidneys, they noted remarkable effects of treatment on both the urine and blood urea. In a case of chronic nephritis of five years' standing, they obtained, within 10 days, abatement of azotemia and an improvement in general condition, which allowed the patient to resume his occupation. In other cases of azotemic chronic nephritis, results were disappointing. The authors report that they are continuing to study the problem of the inconsistency of the therapeutic action.

PIGMENTARY CIRRHOSIS

Besancon, Klotz and their associates treated pigmentary cirrhosis by implantation of pellets of testosterone propionate (500 mg.). In 10 cases there was a noticeable effect on asthenia, weight and aptitude for work. In some cases, after six months one or two more implantations were necessary. There was practically no effect on hepatomegaly or pigmentation; the effect on sexual disorders was variable. Excretion of 17-ketosteroids, which varied from 2 to 4 mg. before treatment, increased slowly and only moderately. The decrease in excretion, habitually associated with testicular hypotrophy and impotentia coeundi, may be related to a testicular disorder or to a metabolic disorder of sexual steroids of hepatic origin, or perhaps the liver ceases to supply the testicle with some sterol that influences the synthesis of testosterone.

PIGMENTARY CIRRHOSIS AND LIPOMATOSIS

A. Abaza, A. Paraf and their co-workers report an interesting observation concerning the relation between the liver and the pancreas, on the one hand, and the hypophysis and gonads, on the other, in the metabolism of water and fats. In a patient with hypertrophic pigmentary cirrhosis associated with a polyglandular deficiency (total impotency for 10 years) biopsy showed a massive siderotic infiltration of the hepatic cells. Thorn's test indicated corticoadrenal deficiency, and 17-ketosteroid excretion was 5.13 mg. The cachectic condition of the patient was accompanied with great fragility of the skin on pressure, but there was neither diabetes nor melanoderma. Besides an adequate diet, vitamins B and C and liver and choline extracts, the treatment included injection every second day of 25 mg. testosterone propionate for 15 days, followed by the implantation of 600 mg.

The results on hepatic deficiency were remarkable; ascites and edema, as well the 10 year impotency, disappeared, and corticoadrenal deficiency was corrected (Thorn's test). The success is due, according to the authors, to the massive doses of testosterone propionate. During the period of clinical improvement of cirrhosis, and coinciding with the administration of testosterone propionate, a symmetric diffuse lipomatosis, which does not affect the neck or face, occurs. There is no fatty infiltration of lymph nodes. The rapidity of onset and the normal level of serum lipids (too high for cirrhosis) in this lipomatosis are suggestive of a latent lipid disturbance of pancreatic origin, associated with a disorder of water metabolism. It is the first time that an action of the testosterone of fat metabolism has been reported. On the other hand, there is also a tendency to water retention, perhaps favored by the existence of an excess of the antidiuretic principles of hypophysial origin, which Ralli, Hall, Stuck and their associates recently emphasized but about which the authors, in this case, were unable to furnish evidence. Notwithstanding this hydrofatty infiltration, which is painless on palpation, and the persistence of induration of the liver, the patient's general condition is good.

Chauffard and Still's Syndrome Controlled with Large Doses of Testosterone.—R. Rivoire and M. Salvadori (Nice) reported on June 9, 1950, at a meeting of the Medical Society of the Paris Hospitals, the case of an 8 year old girl who for three years had had Chauffard and Still's syndrome and in the late stage weighed 8 Kg. Her sedimentation rate was greatly acelerated, and she had severe pain. The condition was controlled with massive doses of testosterone propionate (80 mg. daily); within a few days her temperature fell, the pains subsided and her appetite returned. After six months of treatment, the child walks about normally; she weighs 23 Kg. and has no more swelling of the knee or of the wrist. There persists only painless, slight deformity of the fingers. Despite a few weeks' interruption of treatment, there has been no relapse. The treatment was well tolerated, the appearance of pelvic hair being the only side effect left. The authors decided in favor of treatment with testosterone propionate on the basis of a biologic hypothesis, that in rheumatism there exists a pathological growth factor of steroid structure peculiar to collagen cells, and because cortisone was not available. If a substance of a closely related structure is given, a phenomenon of cellular competition occurs; thus activity would not be limited to a single body but would extend to the whole group of steroid substances. The authors believe that the action of sex hormones in the cancer of the prostate and of the breast may be explained by the principle of cellular competition, endocrinologic application of which is promising.

BELGIUM LIÈGE, Nov. 16, 1950.

Scientific Congress at Katanga.—The Special Committee of Katanga organized a scientific congress on its fiftieth anniversary. Prof. Rodhain, who presided, presented a general summary of human diseases in Katanga in 50 years of European occupation, with discussion of the part played by imported labor. Cholera, plague and yellow fever do not exist in Katanga. Smallpox, once prevalent, has since 1902 practically disappeared. Endemic and epidemic typhus are now rare. The epidemic diseases in the area were typhoid, bacillary dysentery, cerebrospinal meningitis and trachoma. The endemic diseases described by the author were malaria, still common even in the high plateau regions, human trypanosomiasis, tick fever, yaws, leprosy, which is not very prevalent, goiter in the region of Kibara, bilharziasis, filariasis, which, however, is not found in the high plateau regions, acute anterior poliomyelitis, tuberculosis, first observed in 1912, and pneumococcic infections, which are particularly prevalent

among the Negroes of the Congo. The health of the native working population in the high plateau regions is, on the whole, good. A well organized and active hygiene service has produced some remarkable results for them as well as for the Europeans.

Hypoproteinemia was well described by Dr. J. L. Bertrand. If one considered the entire world and not only the so-called civilized countries, one could say that hypoproteinemia is the most widespread disease on the face of the earth. It is the cause and also the effect of the distress of poor and backward populations and is indirectly responsible for their high mortality. In Africa, it is seen especially in young children, who require 3 to 4 Gm. of proteins per kilogram of body weight. The disease is frequently found in breast-fed native infants, if the mother does not have milk in adequate quantity or quality. During the war, the disease referred to as hunger edema, was prevalent in concentration camps. In the Middle Ages, it prevailed among the poor populations of Europe and was responsible for an appalling infant mortality. Without doubt, diet should be the main therapeutic approach, but, if this is not possible, protein hydrolysates should be given intravenously. Dr. Bertrand observed that intramuscular injections of liver extract were helpful, and possibly indispensable, as adjunct treatment.

The future of the European colonists and of the Negroes with regard to the climate of Katanga was considered by Dr. Lejeune. There are three different climatic zones in Katanga, varying from temperate to tropical. Propaganda and general preventive and hygienic efforts are still indispensable for the improvement of conditions for the Negroes. The future of the country depends on the natives, without whom the Europeans would be lost. Accordingly it is necessary that recruiting from distant regions be proscribed and the men be kept in the villages or at least in the district. It is necessary that the growth of towns be controlled and strict measures of general hygiene be maintained in these towns. The physician responsible for health matters, in order to be effective, should have an assistant, a sanitation agent, who would give vaccinations, make out passports and visit boats. Thus, the physician would be relieved of these duties and would be free to consider more important matters. All possible measures should be taken to preserve and increase human resources, both white and Negro.

HISTORY OF SLEEPING SICKNESS

Professor Rodhain recalled the discovery of this sickness in this region in 1904 and 1906. About 1910, Neave stated that Glossina morsitans did not transmit the trypanosomes of sleeping sickness from one human being to another. From a political viewpoint, this was of considerable importance, for it reassured the authorities in Rhodesia, where natives were engaged as workers in Katanga. Treatment became increasingly difficult when resistance to the chemotherapeutic agents developed. Professor Rodhain suggested that the use of new insecticides in the destruction of the Glossina morsitans be studied.

CAMPAIGN AGAINST TUBERCULOSIS

The Cemubac (Medical Center of the University of Brussels in the Congo) organized a tuberculosis detection mission at Maniema-Kivu. Dr. F. Thys cited the most important results. The mission began work in April, 1949; 90,000 persons were examined in one year. The incidence of tuberculosis in general is almost three times that in the mining centers (for example, Saramabila has 4.32 per cent in contrast to Kindu's 12.2 per cent). In a mining center, medical supervision with immediate isolation of persons with tuberculosis offers effective protection against the dangers presented by the tuberculous person, who, in the absence of a health organization, is ignored; therefore, each day he contaminates those around him. The medical center hopes to begin the second phase of the struggle: therapy.

RABIES

Rabies has caused the death of dogs and herbivorous animals and of a number of natives as well. Accordingly, the members of the commission requested that the efforts of the human and veterinary medical services be consolidated for the study of measures for eradication of this disease. Compulsory and repeated vaccination of dogs is being considered.

Lupus League Prize.—The Belgium Royal Academy of Medicine awarded the Lupus League Prize, which was established by this association for outstanding work on the treatment of lupus, to Dr. G. Fanielle of Liège, who was the first to use vitamin D in lupus. Even though vitamin therapy does not cure advanced lupus in all cases, it constitutes a powerful weapon against this form of cutaneous tuberculosis.

SWEDEN STOCKHOLM, Nov. 15, 1950.

Revision of Antiquackery Legislation.—The appointment in October this year by the government of a committee to inquire into antiquackery legislation is an admission that the law of Sept. 21, 1915, on this subject has been inadequate. The committee of five has a majority of laymen on it. Its chairman is a distinguished lawyer, and the rector of the Karolinska Institute (Prof. Hilding Bergstrand) is one of its members. In addition to a doctor with administrative experience, there are two members of the Second Chamber of the Swedish Parliament, a publisher and a woman school teacher. This preponderance of laymen on the committee is a reminder to all concerned that quackery is a matter of deep concern to laymen by no means willing to relegate its solution to the medical profession only.

The law of 1915 provides for the punishment of quacks taking payment for the treatment of venereal disease, tuberculosis, cancer and epidemic diseases. The quack who undertakes treatment involving hypnosis or general anesthesia and entailing danger to life or health is also liable to punishment under this law. But it leaves him a wide field in which to bleed his victims with impunity, and the penalties it has inflicted have often not been very discouraging. By 1941 the authorities were convinced of the inefficacy of this law in the face of the evolution of modern quackery.

Antihistamine Drugs for the Common Cold.—At an aviation center in Arboga, Dr. G. Bergquist has undertaken a carefully controlled study that deflates the claims made on behalf of the antihistaminic drugs as a quick cure for the common cold. This study lasted from December 1949 to the end of May 1950, with observations on 594 persons between the ages of 20 and 60. Dr. Bergquist was able to eliminate from his study all who were known to be allergic. The study began with preliminary daily press notices, in order that the participants should take an intelligent interest in its execution and objects. They were classified in two main groups according to duration of symptoms and to treatment, up to six hours or six to 12 hours. The subjects reported to a nurse, who helped them to fill in forms and issued packets containing tablets marked, respectively, A and B (an antihistaminic drug or inert substance). The participants were not informed of the contents.

The drugs tested were diphenhydramine hydrochloride, tripelennamine hydrochloride and antazoline hydrochloride; the dosage for diphenhydramine, for example, was 30 mg. three or four times a day. The nurse issued the tablets only to persons with a head cold or a sense of irritation in the throat; tablets were not given to patients with definite bronchitis or tonsillitis. Cessation of symptoms within two days of their appearance was interpreted as recovery, spontaneous or in response to treatment. Among the 256 patients treated with diphenhydramine or inert tablets, the recovery rate was 40.5 per cent for the former, and 48.2 per cent for the latter. This paradoxical result, involving only those patients with symptoms lasting less than six hours, was confirmed in patients whose symptoms had lasted six to 12 hours, but in this group the recovery rate was only 20.9 per cent for the subjects receiving diphenhydramine as compared with 22.8 per cent for the controls. Dr. Bergquist, whose investigations were published in the organ of the Swedish Medical Association, *Svenska Läkartidningen*, for Oct. 20, 1950, concludes that antihistaminic drugs are incapable of aborting or curing the common cold and that in about one third of all such cases spontaneous recovery occurs within two days of the onset of symptoms.

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CORRESPONDENCE

CALCIFICATION IN THE SOUTH AFRICAN BANTU

To the Editor:—I read with interest the recent contributions of Dr. Stearns on the requirement of calcium (*J. A. M. A.* **142**:478 [Feb. 18] 1950) and of Professor Youmans on the subject of calcium deficiency (**143**:1252 [Aug. 5] 1950). The need of a high intake of this element has often been emphasized, and it has been stated that in the United States the diet is more likely to be deficient in calcium than in any other element. Yet Professor Youmans maintains that the incidence of calcium deficiency is unknown, and Professor Snapper (in Joliffe, N., and others: Clinical Nutrition, New York, Harper & Brothers, 1950) considers primary deficiency of calcium to be extremely rare. Since misgivings prevail over the level of the calcium intake of a relatively well fed population, such as that of the United States, the question arises as to the state, in terms of calcium deficiency diseases, of the many millions of people in other parts of the world whose diet is greatly inferior in calcifying properties.

In South Africa the calcium intake of the Bantu, especially the town dwellers, can seldom exceed 0.5 Gm. per day. The phosphorus intake, much of it in the form of phytic acid phosphorus, is high, usually more than 1.5 Gm.; moreover, at the times and in the places where maize is the exclusive source of calories, a calcium-phosphorus ratio as unfavorable as 1 to 10 is reached. Practically no vitamin D is ingested.

The present situation, in the light of the information available, is as follows. In East Africa, the Rhodesias and South Africa, rickets is reported to be rare. But the disease is common where urban Bantu are overcrowded, just as it is common in India under the same conditions. In Johannesburg, it occurs more frequently in babies less than a year old, who are mainly breast fed; but it is of rare occurrence after the age of 2. Tetany is considered by experienced clinicians to be uncommon. Bantu mothers are reported not to suffer from osteomalacia. The calcium content of their breast milk, for the few samples examined, has been found to lie within the same range as that of European mothers. Regarding serum levels for calcium and phosphorus, the limited number of determinations carried out suggest that the Bantu have the same or only slightly lower values than Europeans. Ample opportunity for radiologic observation is afforded by many hospitals, for example, those concerned with the quarter of a million Bantu workers employed in the gold mines of the Witwatersrand. The opinion is held that there is no difference in calcific density between the bones of these people and of contemporary Europeans. It is averred that fractures are not unduly liable to occur; there is evidence, moreover, that when these do occur, the rate of healing is, if anything, more rapid than is the case with Europeans. In general, the rural Bantu, when consuming their traditional high cereal diet, have a low incidence of caries, but, as has been reported of primitives elsewhere, when the Bantu adopt European food habits, deterioration begins to take place. The average height of the Bantu is certainly less than that of European South Africans, but, since their diet is frequently unsatisfactory in many respects, not only on account of their low intake of calcium, it is unfair to blame a deficiency of this element as the sole cause. It is of importance, however, that poor European South Africans consume a diet similar to that of the Bantu; yet, reports indicate that the height of the children is not adversely affected thereby. It might also be added that there is evidence that European South African children are, with minor limitations in certain age groups, taller and heavier than their contemporaries in Great Britain, Canada and the United States; yet, their intake of calcium, in general, is below that in the above countries. The very important factor favoring calcification is the sunlight in this part of the world. Can the lack of deficiency stigmas be wholly attributed to this factor?

The information given requires further investigation before being firmly established; to this end, cooperative research work, biochemical, radiological and clinical, is proceeding. Should the above observations be confirmed, the conclusion would seem to be inescapable that, at least where sunlight is plentiful, the critical importance attached by nutritionists to a high intake of calcium is unwarranted.

(This letter is published with the permission of the South African Council for Scientific and Industrial Rsearch.)

A. R. P. WALKER, Ph.D.,
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ROBERT LATOU DICKINSON

To the Editor:—Few persons have contributed more to the art and science of obstetrics in the United States than Dr. Robert Latou Dickinson, and we cannot let the moment of his passing go by without recording our appreciation of him as a great person, doctor, teacher and artist. He was one of the first to warn against the evils of "assembly line obstetrics" to the personality of the mother and father in the normal function of childbearing and to decry the growing trend to make birth a surgical operation.

When Dr. Dickinson retired from active medical practice, he made in the last two decades of his life a unique and important contribution to medical and health teaching. Working with Abram Belskie, a sculptor of great talent, the two developed medical teaching aids in plaster and rubber. The first of these were made for the Maternity Center Association's New York World's Fair exhibit. They depicted in life-size sculptures the development of a baby from the moment of fertilization to the moment of birth. These sculptures were one of the most popular exhibits at the Fair and were later made into a medical teaching book, the "Birth Atlas," which is used in the medical and nursing schools and parents' classes in many countries of the world. Copies of these sculptures are now on exhibit in the New York Museum of Natural History, the Field Museum in Chicago, the Cleveland Health Museum, the Dallas Health Museum and in a number of foreign countries. The rubber models were developed to help the student doctor and nurse and the parent to learn more about the normal human body. Dr. Dickinson's books on a number of subjects related to human reproduction are of worldwide repute. His fearless willingness to take a public position on subjects of controversy won for him the admiration not only of those who agreed with him but of those who disagreed.

I speak for the board, the medical board and the staff of the Maternity Center Association when I say that his passing is an irreparable loss to the dynamic advances in our field of endeavor. But his contribution to medical science and to human relations, especially in the development of mutual understanding between the doctor and his patient, will live forever among the people of America.

MRS. SHEPARD KRECH, President.
Maternity Center Association,
New York, 21.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Malpractice: Application of Res Ipsa Loquitur in Fracture Cases.—The plaintiff filed suit to recover damages resulting from the alleged malpractice of the defendant physician. From a judgment in favor of the plaintiff, the physician appealed to the Supreme Court of Washington.

On July 19, 1947, the plaintiff went to the defendant for treatment of a simple, transverse, greenstick fracture of the radius of the left forearm, and the arm was placed in a cast on that date. The cast was removed on August 26, and the defendant testified that he then felt that he had achieved a satisfactory result in the reduction of the fracture. He said, ". . . the appearance of the arm looked natural, and I felt across this fracture, and you could just barely feel an observable mass, but if you were not looking for it you couldn't see it." He testified further that he fluoroscoped the arm at that time and that the fragments were in good alinement and that "There was a callus formation or calcium deposit present, and it showed union of the bones." A technician who did laboratory and x-ray work for the defendant was present when the arm was fluoroscoped, and the defendant showed him the position of the bones and pointed out that they were in good alinement. Unfortunately no roentgenograms were taken at that time. Two days later the plaintiff consulted another physician who, after an examination of her arm, called the defendant and reported a marked displacement of the radius and said that an open reduction would probably be required. On September 2 the plaintiff returned to the defendant's office at his request. The defendant concedes that on that date the fractured bone was not in alinement and that an open reduction was the proper treatment for the condition then existing. It is undisputed that the situation was corrected by an open reduction and bone graft, bone being taken from the plaintiff's left leg.

The defendant contended that it was incumbent on the plaintiff to establish the material allegations of her amended complaint by medical testimony and that the plaintiff failed to do so. No doctor testified for the plaintiff except the defendant, who was called as an adverse witness.

We have held, said the Supreme Court, that some results of medical care and treatment bespeak negligence so plainly that e. .t testimony is not needed. We have in effect applied the doctrine of res ipsa loquitur to certain malpractice cases; that is, there are circumstances where it can be said that the result speaks for itself. Continuing, the Supreme Court said that if the plaintiff's arm was in the same condition on August 26, when she left the defendant's office, as it was on September 2, when she returned, and she testified that it was, a prima facie case of malpractice seems sufficiently established without expert testimony.

The plaintiff testified that when the cast was removed she immediately noticed that her arm was crooked and had a lump projecting about 1 inch from the top of the arm where it was fractured and that the lump extended in a tapering manner for 3 inches along the top of her arm. She was alarmed at the appearance of the arm, but the defendant said that the lump would disappear within three months. Five other persons also testified as to the condition of her arm. Such condition, said the court, was not the result to be expected from proper treatment of a simple fracture with no complications and the defendant does not contend that it was. His testimony, corroborated by a pharmacist who assisted him in setting the arm and by the x-ray and laboratory technician, was sufficient if believed to establish proper treatment and a satisfactory result. He sought to show that a fall probably caused the misalinement reported on August 28 and shown by the roentgenograms taken on September 2. The issue as to the condition of the arm on August 26 thus became one of veracity. The jury, said the court, was entitled to accept the version of the plaintiff and her witnesses. If her version is true, the result of the treatment was probably a bad one within the rule of the cases heretofore referred to. The Supreme Court concluded that there was sufficient evidence, without expert testimony, to take the plaintiff's case to the jury and to sustain a verdict for the plaintiff. Other contentions of the defendant were also overruled, and the judgment in favor of the plaintiff and against the physician was affirmed.—*Olson v. Weitz, 221 P. (2d) 537 (Wash. 1950).*

Malpractice: Performance of Operation Beyond Scope of Permission.—The plaintiff sued for damages alleged to have resulted from an unauthorized operation performed upon her by the defendant physician. From a judgment in favor of the physician, the plaintiff appealed to the Supreme Court of Washington.

The plaintiff engaged the defendant physician to remove her appendix and straighten the position of her uterus. The plaintiff and her husband had no children, and she was desirous of having nothing done in the course of the operation that would impede a pregnancy. This was made known to the defendant, and he assured the plaintiff he would do nothing other than remove the appendix and straighten the uterus. During the course of the operation the defendant removed the appendix, but he also discovered that the fallopian tubes and one ovary were adhered to the uterus and that there was a cyst on one ovary. He removed the cyst in order to straighten the uterus and separated the tubes and ovary therefrom. In doing so parts of the ovary were also removed.

The evidence indicated, said the Supreme Court, that the plaintiff believed her inability to become pregnant was due to the lack of normalcy in the position of her uterus and that if that difficulty were removed the disability would cease. She contended that the removal of the cyst and part of the ovary by the defendant exceeded the permission which she had granted and might impede future pregnancy.

The plaintiff called as witnesses a pathologist and a physician and surgeon who assisted the defendant in the performance of the operation. They testified that in order to straighten the position of the uterus it was necessary to free the tubes and ovary from their adherence to it, and, in doing so, fragments of the ovary became cut off from their blood supply and had to be removed. They both testified that the amount of ovarian tissue removed would not affect the plaintiff's ability to become pregnant, and the surgeon stated that the plaintiff would have a better chance to become pregnant than she had before the operation.

It is clear, said the Supreme Court, that the defendant did just what he was instructed to do. He removed the appendix and adjusted the uterus to its normal position. The plaintiff wholly failed to prove that the necessary and incidental separating of the adhered tubes and ovary or the removal of the cyst has rendered her unable to become pregnant. All of the evidence which she produced indicates that some unknown condition had existed during all her married life, as a result of which she has not become pregnant. She has not shown that the operation affected that condition one way or the other.

We are in accord with the plaintiff's contention, the Supreme Court continued, that if the defendant performed surgery beyond that which he was directed to perform, he would be liable for any resultant injury or damage. The inhibition was that he should do nothing, in addition to the adjustment, that would prevent pregnancy. The breaking up of the adhesions in order to adjust the uterus was a necessary part of what he was requested to do. The trial court has nothing before it to indicate that the defendant had done anything which was prohibited, but, on the contrary, if any change had been brought about at all it was in the direction of the removal of her disability. Whether the defendant deviated from what he had contracted to do or what plaintiff directed him to do must necessarily depend on medical testimony and that which plaintiff submitted refutes her own claim. Accordingly the judgment in favor of the defendant physician was affirmed.—*Russell v. Jackson, 221 P (2d) 516 (Wash. 1950).*

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MEDICAL LITERATURE ABSTRACTS

AMERICAN

A.M.A. Am. Journal of Diseases of Children, Chicago

80:533-718 (Oct.) 1950

*Treatment of Primary Atypical Pneumonia in Children with Aureomycin: Report of 19 Cases. C. E. Anderson Jr.—p. 533.
Testing of Trend in Bodily Development of School Children. W. Koch and D. Kaplan.—p. 541.
"Tween 20" and Fecal Fat in Premature Infants: Preliminary Study. A. L. Johnson, R. B. Scott and L. H. Newman.—p. 545.
Factors Influencing Retention of Nitrogen and Calcium in Period of Growth: VIII. Influence of Rest and Activity. J. A. Johnston. —p. 551.
*Primary Complex of Pulmonary Tuberculosis. A. D. Biggs.—p. 566.
Respiratory Acidosis in Children with Cerebral, Pulmonary and Cardiovascular Disorders. D. E. Johnstone and E. Bruck.—p. 578.
Friedländer-Aerogenes Infections in Infancy. W. Obrinsky, R. E. Dormont, R. E. L. Fowler and F. Ruhstaller.—p. 621.

Aureomycin in Primary Atypical Pneumonia.—The onset of symptoms in atypical pneumonia is usually gradual, with nonproductive cough and fever. The cough is particularly severe at night, and most of the symptoms are typical of an infection of the upper respiratory tract. Physical examination frequently reveals rales, which are less than would be expected from the roentgen evidence of pulmonary consolidation. A low to normal leukocyte count is the rule. Treatment with sulfadiazine or penicillin is not effective. The appearance in the serum of cold hemagglutinins for human group O cells or agglutinins for Streptococcus MG has been noted in a variable proportion of patients. It was generally agreed until recently that no effective therapy existed for primary atypical pneumonia, although aureomycin has been used in adults with this disease. Anderson reports on 19 children who were given sulfadiazine and/or penicillin for two to three days. They were clinically worse or unimproved. Aureomycin was of great benefit, and its effect was even dramatic in some instances. All the diagnostic tests were performed except serologic studies on serial serum specimens for antibodies against recognized viral or rickettsial agents and studies for development of cold hemagglutinins. This study does not concern the etiology of primary atypical pneumonia.

Primary Complex of Pulmonary Tuberculosis.—The investigations described by Biggs were carried out in a hospital where it is a routine procedure to perform tuberculin tests, both with purified protein derivative and Vollmer patch tests, on patients 1 year of age or older. In each patient with a positive reaction, physical examinations are made at regular intervals; children with new lesions are examined monthly or bimonthly, and those with older lesions, at 3, 6 or 12 month intervals. The examination includes auscultation and percussion of the chest and may be supplemented by blood count, urinalysis, determination of sedimentation rate and gastric washing. Roentgenograms of lesions in the early stages are made monthly, bimonthly or quarterly. During the last eight years the author closely observed 142 children with the ordinary primary complex of pulmonary tuberculosis. More than half were under observation for at least five years. Evidence indicates that for practical clinical purposes the overwhelming majority of these primary tuberculous infections of the lungs in infants and children are entirely asymptomatic. The child's general well-being is not changed by them, and they can be detected only by a combination of skin tests and serial roentgenograms. The latter is the only effective means of observing their progress. The primary complex of pulmonary tuberculosis begins as parenchymal lesions, usually multiple, which drain rapidly into the corresponding hilar nodes. Both the peripheral and central lesions heal slowly, with calcium deposits in the hilus in about 90 per cent of these children. Peripheral calcium deposits or Ghon tubercle formations occur in about 25 per cent. Although the primary infection is rapidly brought under control by the body defenses, the tissue changes, as evidenced by roentgen observation, progress for a period of years rather than months. In the course of this investigation three children with primary infections had some clinical symptoms. The pulmonary lesions in these children cast massive roentgen shadows, and tubercle bacilli were demonstrated by guinea pig inoculation. Children with the ordinary primary complex need no treatment except removal from the source of infection. Those with the massive primary infection should be isolated as long as tubercle bacilli can be recovered from gastric washings.

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Titles marked with an asterisk (*) are abstracted.

A.M.A. Archives of Pathology, Chicago

50:395-518 (Oct.) 1950

Medicolegal Identification of Seminal Stains Using Acid Phosphatase Test. F. Lundquist.—p. 395.
Polycystic Kidney (Mesonephros) in Goldfish. H. G. Schlumberger. —p. 400.
Metabolic Antagonists in Experimental Cancer: Guanazolo. B. Sokoloff, J. B. Redd and R. Dutcher.—p. 411.
Studies on Effect of Radioactive Colloidal Gold on Development of Oral Structures of Mouse. M. S. Burstone.—p. 419.
Nonspecific Periappendical Granulomas. J. E. Musgrove and M. B. Dockerty.—p. 427.
Pathology of Early Amebic Hepatitis: Experimental Study. G. M. Carrera.—p. 440.
Varicella Pneumonitis: Report of Case with Autopsy Observations. L. Frank.—p. 450.
Pathology of Oxyuriasis with Special Reference to Granulomas Due to Presence of Oxyuris Vermicularis (Enterobius Vermicularis) and Its Ova in Tissues. W. St. C. Symmers.—p. 475.

Geriatrics, Minneapolis

5:239-296 (Sept.-Oct.) 1950

*Rheumatic Valvular Disease in the Aged. H. B. Sprague and D. B. Carmichael Jr.—p. 239.
Hazards of Surgery Beyond Age of 80. S. E. Ziffren, L. L. Zager and S. C. Cullen.—p. 252.
Paroxysmal Arrhythmias: Psychosomatic Study. C. H. Duncan and I. P. Stevenson.—p. 259.
Senile Changes in Histologic Structure of Thyroid Gland. P. O. Mustacchi and E. Lowenhaupt.—p. 268.
Reactions Attributed to Administration of Thiamin Chloride. C. G. Weigand.—p. 274.

Rheumatic Valvular Disease in the Aged.—Sprague and Carmichael report on 115 cases of rheumatic valvular disease in 73 men and 42 women between the ages of 50 and 94. Gross pathological criteria included moderate or severe degrees of valvular thickening giving the typical indicative pattern of rheumatic valvular stenosis; gross vascularization of valves in the absence of syphilis or bacterial endocarditis; shortening, thickening and fusion of chordae tendinae with or without papillary muscle fibrosis, and the verrucae of rheumatic valvulitis. Microscopic evidence included Aschoff nodules, left auricular patches of thickened endocardium and typical vascularization of valves. Cases with evidence of bacterial endocarditis at necropsy were included only if valves uninvolved by the septic process revealed stigmata of rheumatic infection or if it was concluded that the acute or subacute

lesion was implanted on a valve showing evidence of previous inflammatory change. Rheumatic heart disease is not uncommon among the aged. The low incidence of childhood rheumatic fever, rarity of recurrence, prolonged life and infrequency of death attributable to rheumatic cardiac involvement suggest either an atypical initial rheumatic infection or a variant of the classical course of rheumatic heart disease. The absence of pronounced cardiac enlargement and the maintenance of a sinus mechanism in the extremely aged may well have been significant factors in prolonged life. If these cases represent an atypical form of rheumatic disease, it is assumed that in the earlier years covered by the authors' series there was mixing of these cases with those presenting the classical clinical course. An active life for a person with rheumatic valvular damage, in the absence of cardiac insufficiency or active rheumatism, appears to have no deleterious effect on the ultimate prognosis. Prolonged periods of congestive failure are seldom seen in the aged patient with chronic rheumatic endocarditis. The added strain of auricular fibrillation, auricular flutter and paroxysmal tachycardias may result in congestive failure in a previously compensated heart. The diagnosis of mitral stenosis, aortic stenosis and bacterial endocarditis in the aged depends largely on the recognition of the possibility of occurrence of these lesions.

Indiana State Medical Assn. Journal, Indianapolis

43:829-976 (Sept.) 1950

Diagnosis of Intracranial Tumor. S. R. Snodgrass.—p. 849.
Treatment of Arthritis. H. C. Coggeshall.—p. 853.
Perforative Appendicitis Complicating Pregnancy of Women with Situs Transversus Viscerum: Case Report. N. F. Richard.—p. 856.
Unusual Physcal Finding in Case of Left Ventricular Aneurysm. J. F. Ling and A. D. McKinley.—p. 860.

43:977-1064 (Oct.) 1950

President's Address. C. S. Black.—p. 997.
Myocardial Infarction Due to Syphilitic Ostial Stenosis: Report of Case. C. Fish and D. Rosenbaum.—p. 998.
Traumatic Injuries to Liver and Spleen. J. K. Berkman and V. V. Lee. —p. 1001.
Causes of Death in Aneurysm of Heart: Incidence of Acute Coronary Artery Thrombosis in Established Cases: Report of Case. W. A. Shullenberger.—p. 1005.
Chronic Recurrent Pancreatitis. T. S. Malinowski.—p. 1010.

Journal of Clin. Endocrinology, Springfield, Ill.

10:989-1176 (Sept.) 1950

Some Notes on Role of Research in Development of Modern Treatment of Exophthalmic Goiter. S. F. Haines.—p. 989.
Iodine Compounds in Blood and Urine of Man. J. E. Rall.—p. 996.
Distribution of Radioactive Iodine in Human Tissues: Necropsy Study in Nine Patients. J. B. Trunnell, B. J. Duffy Jr., J. T. Godwin and others.—p. 1007.
•Evaluation of Radioactive Iodine in Treatment of Hyperthyroidism. R. H. Moe, E. E. Adams, J. H. Rule and others.—p. 1022.
Effect of Isotopic (I^{131}) Radiation and X-Radiation on Total Coproporphyrin Excretion in Humans. H. J. Koch Jr., T. R. Talbot, M. Bernstein and others.—p. 1029.
Appraisal of Radioiodine Tracer Technic as Clinical Procedure in Diagnosis of Thyroid Disorders: Uptake Measurement Directly over Gland and Note on Use of Thyrotropin (T.S.H.). S. C. Werner, H. B. Hamilton, E. Leifer and L. D. Goodwin.—p. 1054.
•Radioactive Iodine in Treatment of Hyperthyroidism of Nodular Goiter. C. E. Richards, G. Crile Jr. and E. P. McCullagh.—p. 1077.
Evaluation of Radioactive Iodine Therapy in Metastatic Thyroid Cancer. V. K. Frantz, W. G. Larsen and A. Jaretzki III.—p. 1084.
Some Surgical Problems of Nontoxic Goiter. L. W. Sloan.—p. 1092.
Indications for Neck Dissection in Carcinoma of Thyroid. R. B. Cattell.—p. 1099.
Thyroglossal Tract Lesions. J. C. McClintock and D. E. Mahaffey. —p. 1108.
New Intralaryngeal Approach for Arytenoidectomy in Treatment of Bilateral Abductor Vocal Cord Paralysis. W. C. Thornell.—p. 1118.
Basal Metabolic Rate and Plasma Cholesterol as Aids in Clinical Study of Thyroid Disease. E. C. Bartels.—p. 1126.
Clinical Determination of Protein Bound Iodine in Plasma. S. B. Barker and M. J. Humphrey.—p. 1136.
Natural and Experimental Alteration of Thyroid Function in Domestic Animals. F. N. Andrews.—p. 1142.
Cancer of Thyroid. G. Crile Jr.—p. 1152.

Radioactive Iodine in Treatment of Hyperthyroidism.—Moe and co-workers treated 100 patients with hyperthyroidism with radioactive iodine (I^{131}). There was satisfactory remission in 88 patients, 57 with diffuse goiter and 31 with nodular goiter. The basal metabolic rate of the patients with diffuse goiter dropped from an average of +32.8 to +2.4 per cent after an average total dosage of 5.6 millicuries. The patients with nodular goiter showed an average reduction in basal metabolic rate from +35 to +7.6 per cent, after an average total dosage of 11.7 millicuries. Nine patients, eight with diffuse goiter and one with nodular goiter, became hypothyroid. The basal metabolic rate of the patients with diffuse goiter in this group was lowered from +36.4 to —18.2 per cent after an average total dosage of 4.9 millicuries. The basal metabolic rate of the patient with a nodular goiter dropped from +42 to —19 per cent after the administration of 5.4 millicuries. The remaining three patients, two with diffuse goiter and one with nodular goiter, became myxedematous. They received a total dose of 1.2, 5.1 and 4.6 millicuries of radioactive iodine respectively. After one dose, 26 patients with diffuse glands had a satisfactory response, 18 required two doses and 11 received three. Two patients with severe hyperthyroidism and large diffuse glands were given five doses before a satisfactory remission was effected. Only nine of the 31 patients with nodular goiter had satisfactory remissions with one dose, 10 were given two and 12 required three to five doses. Of the 12 patients in whom hypothyroidism or myxedema developed, 11 received only one dose; the other was given three doses. Forty-nine patients were followed for more than six months and 18 for a year or longer. No recurrence had been observed to date. There was no radiation sickness and no evidence of bone marrow depression or injury to the parathyroids or kidneys. Increase in exophthalmos was not observed, and a definite improvement was noted in a few cases. The incidence of hypothyroidism and myxedema is comparable to that following surgical intervention. Results suggest that radioactive iodine is a valuable agent in the treatment of selected cases of hyperthyroidism.

Radioactive Iodine in Nodular Goiter.—Richards and co-workers treated with radioactive iodine 37 patients with hyperthyroidism arising in nodular goiters. After the administration of varying amounts of this isotope, 32 patients have had remissions of their disease. The average dose of radioactive iodine required to effect a remission was 37.3 millicuries. The average basal metabolic rate before treatment was +39 per cent. In each instance the patient noted that the thyroid gland had decreased in size. In none of the patients did the goiter completely disappear. Five patients followed six months or longer did not have a remission when last seen. The authors believe that treatment with radioactive iodine may be an acceptable type of treatment in selected patients in the older groups with small nodular goiters, in persons who may be poor surgical risks and in persons who are definitely averse to operation. The total dosage of radioactive iodine in treatment of hyperthyroidism of nodular goiter depends to a greater extent on the size of the gland than on the severity of the disease. Most of the patients with nodular goiter treated with radioactive iodine needed larger amounts of the iodine than have usually been necessary for production of remissions in toxic diffuse goiter.

Journal of Investigative Dermatology, Baltimore

15:157-264 (Sept.) 1950

High Frequency Square-Wave Current in Dermatology: Epilation, Iontophoresis, Cutaneous Sensory Threshold: Preliminary Report H. Sigel.—p. 167.
Primary Familial Xanthomatosis and Biliary Xanthomatosis (Biliary Cirrhosis with Xanthomatosis): Electrophoretic Studies. W. F. Lever and J. G. MacLean.—p. 173.
Protein Studies in Scleroderma. Co Tui, N. H. Kuo and S. Simuangco. —p. 181.
Experimental Histoplasmosis of Skin and Mucous Membranes in Rabbits. E. L. Hazen and E. D. Tahler.—p. 205.
Proteins in Pemphigus Vulgaris: III. Effect of Infusions of Human Serum Albumin on Proteins in Blood Serum of Patients with Pemphigus Vulgaris. W. F. Lever and J. G. MacLean.—p. 215.
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Further Studies of Agglutination and Inhibition in Le^a-Le^b System. O. J. Brendemoen.—p. 335.

°Transmission of Hemolytic Streptococcal Infections in Infant Wards with Special Reference to "Skin Dispersers." C. G. Loosli, M. H. D. Smith, J. Cline and L. Nelson.—p. 342.

Serologic Studies of Mumps Employing Complement Fixation and Agglutination-Inhibition. A. E. Feller and W. S. Jordan.—p. 360.

°Relationship of Complement-Fixing and Antihemagglutinating Factors Against Viruses of Mumps and Newcastle Disease. W. S. Jordan and A. E. Feller.—p. 369.

Preservation of Specific Agglutinability of Human Red Blood Cells. R. L. Wall, M. Jayne and J. Beauchamp.—p. 378.

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Problem of Aspirin Allergy with Report on Skin Testing with Salicylate-Containing Human Sera. K. P. Mathews, R. G. Lovell and J. M. Sheldon.—p. 416.

Observations on Intravenous Administration of Saccharated Oxide or Iron in Human Beings. D. L. Horrigan, J. F. Mueller and R. W. Vilter.—p. 422.

Absence of Respiratory Change or Manifest Tetany with Elevation of Plasma p_H Produced by Bicarbonate Administration in Dogs. C. D. West and S. Rapoport.—p. 428.

Blood Volume in Chronic Leucemia as Determined by P^{32} Labeled Red Blood Cells. N. I. Berlin, J. H. Lawrence and J. Gartland.—p. 435.

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Index of Thyroid Function: Estimation by Rate of Organic Binding of I^{131}. G. E. Sheline and D. E. Clark.—p. 450.

Use of Radioactive Iodine, Radioactive Phosphorus, and Radioactive Sodium in Determination of Cerebral and Muscle Clearance. J. B. Boatman, T. R. Kendrick, F. R. Franke and C. Moses.—p. 456.

Studies on L-Nor-Epinephrine: Relation of Dosage to Pressor and Bradycardia Effect. G. C. Sutton, A. Kappert, A. Reale, C. H. Skoglund and G. Nylin.—p. 460.

Potency Variation in Rabbit Lung Thromboplastic Suspensions. S. Gollub, F. E. Kaplan and D. R. Meranze.—p. 463.

Hemolytic Streptococcic Infections in Infant Wards.—Loosli and co-workers report on the spread of group A, type 33, streptococcic infections in infants' wards of Johns Hopkins Hospital during the fall and winter months of 1945 and 1946. The source of the Streptococcus was a female infant aged 6 months with an infection of the skin superimposed on an infantile eczema. During her stay in the hospital, she contaminated the ward environment, namely, air, dust and bedclothes, with group A, type 33 Streptococcus to a high degree. Secondary streptococcic infections (throat, skin and wound) occurred in 25 infants and secondary streptococcic pharyngeal infections occurred in 18 adults, including attending personnel and visitors. The path of the spread was from the "skin disperser" to the bedclothes, to the air and dust, then to other infants and to attending personnel and visitors. Triethylene glycol vapor did not prevent the dispersion of streptococci through the ward. Treatment of the skin-infected patients and a patient with draining otitis media with penicillin by intramuscular route promptly brought the infections under control. Simultaneously, the ward environment became essentially free of hemolytic streptococci. Antibiotics employed both therapeutically and prophylactically should be considered in any program for the control of secondary infections in hospital wards. Infants and children with streptococcic infections of the skin are dangerous dispersers of these organisms. They should be isolated promptly, cared for by aseptic procedures and treated with suitable antibiotics to inhibit the dispersal of organisms.

Complement-Fixing and Antihemagglutinating Factors.—Jordan and Feller examined single serums from healthy persons and acute and convalescent phase serums from persons with mumps or with other virus or presumed virus infections for heat stable factors capable of reacting with Newcastle disease virus. Complement fixation and agglutination inhibition tests were used in the study of paired serums. A heat stable factor with complement-fixing as well as antihemagglutinating activity against Newcastle disease virus increased in titer in the serums of 12 of 15 patients convalescing from mumps at the same time that there was an increase in titer of mumps antibody. Similar increases in titer were not observed in convalescent phase serums from patients with a variety of other diseases. A slight increase in complement-fixing activity against Newcastle disease virus, in the absence of mumps antibody, occurred in serums from a patient with acute pericarditis. Serums from 98 persons were tested for complement-fixing activity against both mumps virus and Newcastle disease virus. Of the 98 persons, 74 had mumps antibody, 32 had Newcastle disease virus factor and 21 had neither. Of the 32 persons with Newcastle disease virus factor, 29 (included in the 74) also had mumps antibody. Newcastle disease virus factor was detected in three serums in the absence of demonstrable mumps antibody. Although complement-fixing activity against Newcastle disease virus may be observed in serums independent of activity against mumps virus, the close correlation of the two strongly suggests that the presence of Newcastle disease virus factor was dependent on the presence of mumps antibody. The relation is best explained by the assumption that mumps virus and Newcastle disease virus have a common antigen, or antigens, and that Newcastle disease virus factor developed as a response to infection with mumps virus. The serologic diagnosis of Newcastle disease in man must be made with caution.

Journal-Lancet, Minneapolis

70:313-370 (Sept.) 1950

Some Common Medical Emergencies and Their Treatment. R. B. Radl.—p. 313.

Management of Arteriosclerosis Obliterans in Cold Climates. G. A. Kernwein.—p. 318.

70:371-400 (Oct.) 1950

Palliative Radiation Therapy in Neoplastic Disease. K. W. Stenstrom and J. Friedman.—p. 371.

Diagnosis and Treatment of Hyperthyroidism. W. A. Stafne, L. E. Wold and A. C. Kohlmeyer.—p. 378.

Application of Insulins in Treatment of Diabetes Mellitus. L. J. Palmer.—p. 386.

Cortisone and ACTH in Rheumatic Fever. F. H. Adams and P. F. Dwan.—p. 389.

•Clinical Study of Physostigmine Preparations in Relief of Muscle Spasm and Pain. W. Marshall.—p. 391.

Rat-Bite Fever Due to Streptobacillus Moniliformis: Report of Case Occurring in Minnesota. E. R. Hayes, E. G. Kidd and D. W. Cowan. —p. 394.

Diagnosis and Treatment of Hemangiomas. C. W. Laymon.—p. 396.

Physostigmine for Muscular Spasm and Pain.—It has been demonstrated that when the clinical effects of physostigmine are modified by simultaneous use of atropine, there is also an effect on skeletal muscle, although it had been thought previously that physostigmine acted solely on smooth muscle. Marshall tried this combination in the treatment of patients with arthritis and myositis. He used an aqueous or oil solution. One cubic centimeter of the aqueous solution contained 0.6 mg. each of physostigmine salicylate and atropine sulfate in isotonic solution of sodium chloride. It was administered intramuscularly in doses of 1 cc. Each cubic centimeter of the oil solution contained 1.2 mg. of physostigmine salicylate and 1.2 mg. of atropine sulfate, in sesame oil. This was administered intramuscularly in 0.5 cc. doses. The author presents observations on 52 patients whose rheumatoid symptoms were of at least 18 months' duration and who had received at least three injections. The majority were in middle age. The chief complaints were pain and swelling of joints, difficulty in motion and general malaise. All had previously received treatment for arthritis. Some had received injections of gold compounds, others bee venom and still others had been given sulfonamide drugs. Most of them had received salicylates and some form of physiotherapy. Ten per cent of these patients were bedfast, the remainder ambulatory. In 90 per cent of the patients the pain was rated as severe, and 75 per cent had swelling of a joint. The total number of injections varied from three to 50. Most of the patients were farmers and laborers, and many had lived on an inadequate diet. The administration of the solution containing physostigmine and atropine (phyatromine®) was generally followed by prompt relief. After relief from muscle spasm, there was a decrease in tenderness of the soft structures about the joint and in acute cases a decrease in swelling. Relaxation of muscle spasm apparently prevents the develop-

ment of deformities, and, if they already exist, they may be lessened, depending on the severity of the existing fibrosis and ankylosis. An improved mental attitude and better nutrition often become apparent after reduction of pain and after improved articular function. Succeeding injections give the patient more sustained relief than do the first injections. Administration of a solution of phyatromine* to patients with muscular strains due to trauma gives relief. There is no evidence that a solution of physostigmine and atropine benefits the arthritic process per se, but it gives palliative relief, permitting the patient to recover the use of affected muscles and joints.

Journal of Neurophysiology, Springfield, Ill.

13:321-388 (Sept.) 1950

Central and Reflex Regulation of Motility of Pyloric Antrum. B. P. Babkin and W. C. Kite Jr.—p. 321.
Gastric Motor Effects of Acute Removal of Cingulate Gyrus and Section of Brain Stem. B. P. Babkin and W. C. Kite, Jr.—p. 335.
Inhibition of Knee Jerk from Tendon Spindles of Crureus. G. P. McCouch, I. D. Deering and W. B. Stewart.—p. 343.
Reflex Self-Regulation of Muscle Contraction and Autogenetic Inhibition. R. Granit.—p. 351.
Some Physical and Pharmacological Factors Affecting Delayed Response Performance of Baboons Following Frontal Lobotomy. K. H. Pribram. —p. 373.
Electrocorticographic Effects of Stimulation of Posterior Orbital, Temporal and Cingulate Areas of Macaca Mulatta. M. A. Lennox, R. H. Dunsmore, J. A. Epstein and K. H. Pribram.—p. 383.

New Orleans Medical and Surgical Journal

103:101-140 (Sept.) 1950

Treatment of Rheumatoid Arthritis with Particular Reference to Use of Cortisone and ACTH. J. M. McMahon.—p. 101.
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Postpartal Psychotic Reactions. H. P. Harrs Jr.—p. 109.
Treatment and Prevention of Cardiovascular Emergencies. H. H. Cutler and J. D. Kelly.—p. 112.
Prophylaxis of Intravascular Clotting by the Use of Alpha Tocopherol and Calcium. J. H. Kay, G. Balla, S. B. Hutton and A. Ochsner. —p. 116.
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Consderations in Diagnosis of Ectopic Pregnancy. C. G. Callender. —p. 128.

New York State Journal of Medicine, New York

50:2223-2350 (Oct. 1) 1950

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Elusive Mental Cases: Marital Conflicts. B. Liber.—p. 2287.
Aortic Embolectomy in "Buttonhole" Mitral Stenosis. J. J. Silverman and E. S. Hurwitt.—p. 2289.
Treatment of Pneumonia with Single Oral Dose of Penicillin-Sulfadiazine-Sulfamerazine Combination. H. Vollmer, H. H. Pomerance and I. K. Brandt.—p. 2293.
Evaluation of Perazil, New Antihistaminic. A. D. Spielman.—p. 2297.
Prophylactic Value of Papaverine in Insulin Shock Therapy. H. I. Russek, B. L. Zohman and S. L. Tamarin.—p. 2299.
Rapid Administration of Blood by Use of Gravity and Large-Bore Needles. V. Ginsberg and M. R. Marsh.—p. 2302.

Philippine Medical Association Journal, Manila

26:287-338 (July) 1950. **Partial Index**

"Flumamine" New Synthetic Analgesic and Anti-Flu Drug. E. Y. Garcia.—p. 287.
Progress of BCG Vaccination in the Philippines. S. Bona de Santos. —p. 295.
Joint Cooperative Program for Control of Venereal Disease in the Philippines. F. Z. Cruz.—p. 307.
Synergistic Action of Chaulmoogra and Sulfone Drugs. J. G. Tolentino. —p. 315.
Acute Appendicitis in Children. A. I. Reyes and A. A. Pascual.—p. 325.

Psychosomatic Medicine, New York

12:277-342 (Sept.-Oct.) 1950

Screening Patients for Nasal Plastic Operations: Some Sociologic and Psychiatric Considerations. F. C. Macgregor and B. Schaffner. —p. 277.
Possible Etiologic Relevance of Personality Factors in Arterial Hypertension. G. Saslow, G. C. Gressel, F. O. Shobe and others.—p. 292.
Electrical Resistance of Skin During Induced Emotional Stress: Study of Normal Individuals and of Patients with Internal Disease. J. M. van der Valk and J. Groen.—p. 303.
Psychologic Conflict and Neuromuscular Tension: I. Preliminary Report on Method, as Applied to Rheumatoid Arthritis. L. A. Gottschalk, H. M. Serota and L. B. Shapiro.—p. 315.
Psychosomatic Aspects of Salivary Activity: II. Psychoanalytic Observations Concerning Hypersalivation. T. S. Szasz.—p. 320.

Southern Surgeon, Atlanta, Ga.

16:837-932 (Sept.) 1950

Anorectal Surgery—Pre and Postoperative Care. I. E. Harris Jr. and A. I. Dodson Jr.—p. 837.
Congenital Right-Sided Diaphragmatic Hernia in Children. G. T. Howard Jr.—p. 842.
Simultaneous Dislocation of Both Shoulders. I. H. Rapp and C. A. Zarzecki.—p. 852.
Acute Suppurative Mesenteric Lymphadenitis with Peritonitis: Report of Case. J. C. Read.—p. 855.
Carotid Body Tumors: Case Report and Discussion. B. P. Rentz, A. W. Wood Jr. and D. A. Osman.—p. 860.
Traumatic Avulsion of Skin of Shaft of Penis and Scrotum: Report of Four Cases. E. C. Gay and G. P. Oates.—p. 870.
Cystadenoma of Pancreas. T. M. Johnson and D. M. Gibson.—p. 878.
Splenectomy: Indications and Results. R. W. Williams, R. W. Postlethwait, H. H. Bradshaw and L. W. Hutaff.—p. 885.
Multple Fractures in Same Patient. W. G. Stuck, M. S. Thompson and J. K. Tillotson.—p. 898.

Surgery, St. Louis

28:461-620 (Sept.) 1950

Intravascular Agglutination of Erythrocytes (Sludged Blood) and Traumatic Shock. R. O. Heimbecker and W. G. Bigelow.—p. 461.
Experimental Cardiac Surgery: I. Observations on Action of Pump Designed to Shunt Venous Blood Past Right Heart Directly into Pulmonary Artery. W. H. Sewell Jr. and W. W. L. Glenn.—p. 474.
Fibrosarcoma of Soft Tissues of Extremities: Review of 78 Cases. J. C. Ivins, M. B. Dockerty and R. K. Ghormley.—p. 495.
Experimental Evidence of Factors Concerned in Eventual Recovery of Strangulated Intestine: Effects of Massive Penicillin Therapy. H. Laufman.—p. 509.
*Treatment of Staphylococcic Meningitis, with Review of Literature and with Particular Reference to Results with Bacitracin: Report of Five Cases. P. Teng and F. L. Meleny.—p. 516.
Method of Producing Experimental Infected Long Bone Fractures and Their Treatment with Penicillin and Bone Grafting. A. H. Johnson, J. M. Edmiston, H. J. McCorkle and H. Warmer.—p. 534.
Esophageal Anastomosis: Types and Methods of Suture. R. W. Postlethwait, W. R. Deaton Jr., H. H. Bradshaw and R. W. Williams. —p. 537.
Management of Pleural Tears During Thoracoplasty. E. Michelson. —p. 543.
Effect of Vagotomy on Intestinal Activity. S. Faik, J. H. Grindlay and F. C. Mann.—p. 546.
Chlorophyll as Adjunct in Management of Permanent Colostomy. J. M. Goodman.—p. 550.
Effects of Hypochloremia upon Renal Function in Surgical Patients. I. M. Ariel and F. Miller.—p. 552.

Treatment of Staphylococcic Meningitis with Bacitracin.—Teng and Meleney review the history of the treatment of staphylococcic meningitis. Results of therapy were generally poor until the advent of bacteriophage, the later sulfonamides and the antibiotics. Since then, treatment has been increasingly successful. During the last two years, through centers studying the indications for the use of bacitracin, five patients with staphylococcic meningitis have been treated with this antibiotic. All these patients had been treated unsuccessfully with other chemotherapeutic and antibiotic agents. Bacitracin, used after other measures had failed, was clearly effective in every one of these cases. All recovered completely. Experimental and clinical data indicate that the intracranial, intraventricular and intrathecal injection of bacitracin is far less toxic than are the other antibiotics and chemotherapeutic agents that have been tried.

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Annals of Rheumatic Diseases, London

9:209-280 (Sept.) 1950

*Chronic Absorptive Arthritis or Opera-Glass Hand: Report of Eight Cases. W. M. Solomon and R. M. Stecher.—p. 209.
Experiments in Gold-Testing in Gold Treatment of Polyarthritis. T. Svanberg.—p. 221.
Study of Interrelations of Rheumatoid Arthritis and Diabetes Mellitus. K. A. J. Järvinen.—p. 226.
Ankylosing Spondylitis in Sisters. T. N. Fraser.—p. 231.
Further Anatomical Check on Accuracy of Intra-Articular Hip Injections in Relation to Therapy of Coxarthritis. M. M. Dobson.—p. 237.
Investigations of Creatine Excretion in Urine of 38 Untreated Ambulant Male Patients with Fibrositis, and in Two Healthy Men. O. Sylvest and N. Hvid-Hansen.—p. 241.

Chronic Absorptive Arthritis.—Solomon and Stecher say that the term opera glass hand, *la main en lorgnette*, has been used only occasionally, but the disease to which it refers is not as rare as is usually assumed, the same disorder having been described under such terms as psoriatic arthritis, arthritis mutilans and arthritis deformans. Marie and Levi in 1913 described a woman who had had generalized rheumatoid arthritis for 28 years. Her fingers and wrists were shortened and contracted, and the skin was wrinkled and lay in transverse folds, so that the phalanges seemed to be retracted one into the other like an opera glass. The authors describe eight personally observed cases of this disorder. The age of onset ranged from 15 to 35 years, but the age at which the severe absorptive changes began and their exact duration were not known. They were observed as early as three years after onset in one case and have persisted as long as 42 years in a woman 67 years old. Two patients showed changes of the fingernails and skin suggestive of psoriasis. The nails were rough, thick, irregular, friable and separated from the nail bed. The state of the finger and toe joints in this condition varies considerably from the usual observations in rheumatoid arthritis. In the typical rheumatoid arthritic, the joints have limited motion or ankylosis, and the skin over the joints is usually contracted, thin, atrophic, pale and shiny and appears to be firmly attached to the bone. In contrast, most of the finger joints of the patients with opera glass hand have an abnormal range of motion in all directions; the fingers are elongated like a telescope when pulled out; the skin is loose, wrinkled and thickened. The absorption of bone is not that observed in rheumatoid arthritis, for, although most rheumatoid arthritics do demonstrate absorption to a varying degree, in these cases this process has advanced to extreme destruction, with a loss in some instances of as much as half a bone. The process is confined to only one or two anatomic regions, with the other joints showing the characteristic changes of rheumatoid arthritis. Thus, the loss of localized bone substance, the absence of fibrous contracture of the joint capsule and muscle tendons and the flabbiness of the skin produce a picture that may be considered either as an unusual variant or as an extreme manifestation of rheumatoid arthritis.

British Journal of Urology, London

22:165-264 (Sept.) 1950. **Partial Index**

Neoplasms of Epididymis: Review with Report of Two New Cases. S. Glaser.—p. 178.
Genital Tract Tumors of Adenomatoid Nature. J. P. Wyatt and P. S. H. Khoo.—p. 187.
*Intravenous Urography in Renal Tuberculosis. N. O. Ericsson and Å. Lindbom.—p. 201.
Massive Hydronephrosis Presenting as Abdominal Emergency. R. Burkitt. —p. 208.
Testes as Contents of Hernial Sacs in Two "Female" Children. J. Cook. —p. 211.
Value of Penicillin After Operations on Bladder. A. V. Pollock.—p. 214.
Streptomycin in Urinary Tuberculosis. A. Jacobs and W. M. Borthwick. —p. 238.

Intravenous Urography in Renal Tuberculosis.—Ericsson and Lindbom enumerate the drawbacks of retrograde pyelography that induced them to use the intravenous method. They describe the technic they used in the examination of 154 patients with 173 tuberculous kidneys. In nearly all early cases in which the renal function was not greatly impaired, they were able to obtain visualization with this technic which equalled and sometimes surpassed retrograde pyelography. They believe that intravenous urography is the best method of roentgen examination in renal tuberculosis, because it also permits the study of the excretory function. The ureters were visualized with intravenous urography in 80 per cent of the cases, and they showed pathological changes in more than half of these. The commonest sign is ureteral dilatation. This is the earliest sign of ureteritis and may, in some cases, be due to a loss of tonicity caused by a nonspecific inflammation accompanying the tuberculous process in the kidney. Swelling of the interureteral ridge may prove to be a sign of ureteritis and possibly an aid in the diagnosis of renal tuberculosis.

British Medical Journal, London

2:849-902 (Oct. 14)1950

*Study of Cortisone and Other Steroids in Rheumatic Arthritis. W. S. C. Copeman, O. Savage, P. M. F. Bishop and others.—p. 849.
*Insulin and E. C. T. in Treatment of Rheumatoid Arthritis: Report on Pilot Series of Cases. G. D. Kersley, L. Mandel, M. R. Jeffrey, M. H. L. Desmaris and E. Bene.—p. 855.
Effect of Cortisone on Cardiogram in Chronic Adrenal Insufficiency. W. Sommerville.—p. 860.
Further Observations on Age of the Menarche. D. C. Wilson and I. Sutherland.—p. 862.
Fatal Case of Acute Porphyria in a Negro. C. A. Wiggins.—p. 866.
Follow-Up of Rhesus-Negative Primigravidae: Development of Rhesus Immunization. W. Weiner and J. L. Hallum.—p. 868.
Mongolism in One of Twins. T. H. Crozier and W. A. B. Campbell. —p. 869.

Cortisone and Other Steroids in Rheumatoid Arthritis.—Copeman and his associates compared the results of administration of cortisone in five patients with rheumatoid arthritis with the results obtained in 35 patients treated with other steroids. Cholesterol was used as a control substance in the five patients treated with cortisone. Although the patient did not know at the time of administration which compound was being used, the dramatic clinical effects of cortisone were immediately obvious. The other steroid compounds used were androstenedione, dehydroisoandrosterone, progesterone, pregnenolone and pregnadienolone. These proved ineffective, except in one patient treated with progesterone in whom there was a remission of symptoms. However, this success was not repeated when a second course was administered.

Insulin and Electric Convulsion Therapy in Rheumatoid Arthritis.—Kersley and his collaborators point out that insulin has been used as a "tonic" and as a method of increasing weight in rheumatoid arthritis. The more recent theories of the part played by the pituitary adrenal mechanism in this disease suggested another reason for this type of therapy. Cannon and associates found in 1924 that insulin hypoglycemia provoked the liberation of epinephrine, and since then evidence has been produced that shows that the adrenal cortex can be stimulated in this way. The authors treated a group of patients with active rheumatoid arthritis by inducing insulin hypoglycemia, and they treated another group with electric convulsion therapy. Insulin hypoglycemia was induced in forty patients with active rheumatoid arthritis five times weekly for three or four weeks. Of these, 22 showed pronounced clinical improvement, nine slight improvement, eight no change and the condition of one deteriorated. Ten maintained pronounced improvement and three moderate improvement, six weeks after completion of the treatment. In patients showing definite improvement this usually began within a week of the start of treatment. All patients showed an increase in weight. The serum potassium was lowered in 34 of 36 cases at the height of hypoglycemia and had risen again four and a half hours later, at the time of maximal eosinopenia. Urinary uric acid excretion was significantly raised in 11 cases during treatment, but there was no increase in the neutral 17-ketosteroids in the eight cases in which these were estimated. The sedimentation rate was not significantly changed. Fourteen patients showed an increase, and three showed a decrease of more than 1 Gm. per 100 cc. of body surface in hemoglobin. A significant fall in circulating

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

eosinophils four and a half hours after maximal hypoglycemia was shown by 34 patients. There was no definite correlation, however, between the degree of fall and the degree of hypoglycemia or the clinical improvement. Eleven patients were treated by electroshock therapy, with an average of five shocks each. Three showed much improvement, three slight improvement and five no change. No significant fall of eosinophil count was found as the result of electroshock therapy.

Paris Médical

40:479-490 (Sept. 9) 1950

*Neurological Manifestations of Acute Porphyria: Clinicosynthetic Assay. M. Bonduelle.—p. 479.
Acute Condition of the Abdomen Due to Porphyria. R. Claisse.—p. 486.

Neurological Manifestations of Acute Porphyria.—Bonduelle reports the occurrence of polyneuritis associated with severe mental disturbance in a woman aged 40 with acute porphyria. The polyneuritic syndrome was of quadriplegia type and was more pronounced in the lower extremities. There was total symmetric amyotrophy. The patellar and Achilles tendon reflexes were absent. Vasomotor disturbances of the extremities were manifested by profuse sweating, bluish discoloration and brittleness of nails. Sphincter control was retained. The motor syndrome and the mental disturbance, manifested by complete amnesia and aggressiveness, dominated the clinical picture. The history revealed a nearly permanent condition of physical and psychic asthenia, starting at the time of adolescence, with repeated exacerbations. Digestive disturbances with severe pain and vomiting were frequent, as were short attacks of headache. After the patient had an attack of violent abdominal pain associated with refractory constipation, an operation was performed, in the course of which unilateral ovariectomy was done for an ovarian cyst. Attacks of abdominal pain recurred. An acute attack of porphyria was suggested by the polyneuritic syndrome associated with mental disturbance and the absence of any causative factor, although the color of the urine was normal. A ratio of porphyrins amounting to 600 gamma per liter was determined in the urine. Study of the patient's family did not reveal any pathological accident in the first generation. The second generation comprised the patient and four others, three of whom had unstable personalities, headaches, digestive disturbances characterized by short attacks of pain and diarrhea or constipation. The third generation consisted of four children who had no pathological manifestations, but three of whom had a weak positive reaction for porphobilinogen and a porphyrin ratio varying between 200 to 100 gamma per 1,000. Two of the children, the sons of the patient, were monozygotic twins. Acute porphyria is a chronic disease with neurological and digestive manifestations of a congenital and hereditary disturbance of metabolism, the essence and mechanism of which is unknown. Polyneuritis seems to be the most frequent manifestation of acute porphyria and constitutes the most coherent neurological syndrome. Asthenia, instability, irritability associated with insomnia, and frequent attacks of headache constitute the psychic basis of acute porphyria.

Presse Médicale, Paris

58:1029-1044 (Sept. 30) 1950

*Some Considerations on Diagnosis of Tumors of the Breast. H. Redon.—p. 1029.
*Clinical Investigation of Enzymatic Hydrolysis of Acetylsalicylic Acid (Aspirin). D. Vincent and M. Parant.—p. 1030.
"In Vitro" Test of Tolerance to Heparin for Control of Treatment with Bishydroxydicoumarin (Dicumarol®). J. P. Soulier and A. G. Le Bulloch.—p. 1031.

Diagnosis of Breast Tumors.—According to Redon, the large scale campaign against cancer was responsible for the creation of cancerophobia in some patients, although it also induced many others to consult a physician in the earliest stages of the disease. The presence of axillary adenopathy is not essential for diagnosis of cancer of the breast, since involvement of axillary lymph nodes may be a late, secondary symptom. Benign mammary lesions may be associated with adenopathy. The presence or absence of enlarged axillary nodes, therefore, is not a criterion of a benign or malignant lesion except when progressive growth of a tumor is manifested by enlarged fixed lymph nodes. With the exception of cases of bilateral, symmetric, diffuse mastopathy, all patients in whom cancer is suspected should be subjected to a radical operation. Radical excision with strict hemostasis may be less hazardous than partial removal of the tumor or even biopsy, when either is performed on a tumor with a progressive course. Several irradiation treatments may precede surgical intervention in cases in which the clinical picture suggests malignancy. There is an increasing incidence of cancer of the breast with a pseudoinflammatory aspect, a highly acute type with a progressive course. Surgical treatment is contraindicated in cases of this type, because it is ineffective and rather accelerates the fatal course of the disease.

Enzymatic Hydrolysis of Acetylsalicylic Acid.—According to Vincent and Parant, acetylsalicylic acid is split up into salicylic acid and acetic acid in the human organism as the result of the hydrolytic effect of an esterase. The kidney, the liver and the blood serum are active in this hydrolytic process. Comparative studies of the effect of various inhibitors, such as physostigmine and sodium arsanilate, on the hydrolysis of acetylsalicylic acid and acetylcholine by the liver and by the blood serum showed that cholinesterase, which is responsible for the hydrolysis of acetylcholine, differs from the enzyme that is responsible for the hydrolysis of acetylsalicylic acid. Determination by titration of the hydrolytic activity of 150 human serums of normal persons and of patients with various diseases revealed a pronounced drop in the enzymatic action of the serum (acetylsalicylic acid esterase) in patients with cirrhosis, tuberculosis and cachexia. An increase in the enzymatic effect of the serum was revealed in patients with diabetes mellitus, hypertension and plethora as compared with the enzymatic effect of the serum on the acetylsalicylic acid in normal persons. Comparative determination of the enzymatic action of the same 150 serums on acetylcholine showed a general parallelism between the two enzymatic activities, although the two ferments concerned are not identical. The demonstrated hydrolytic effect of some esterase on the acetylsalicylic acid is of much interest pharmacologically, as it offers an explanation for the relatively transient effect of the drug. Combination of acetylsalicylic acid with other substances that may inhibit the hydrolytic effect of the esterase might possibly prolong the effect of the drug on the human organism.

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38:77-148 (July 31) 1950. **Partial Index**

*Monocytic Leukemia: Seven Cases. C. Jiménez Díaz, A. Morales Pleguezuelo and G. Paniagua Rodríguez.—p. 89.

Monocytic Leukemia.—Jiménez Díaz and collaborators report seven cases of pure monocytic leukemia. The disease was malignant and rapidly fatal. Autopsy was done on five. The clinical symptoms of monocytic leukemia are those of acute hyperplastic gingivitis, hemorrhagic lesions of the buccal mucosa, the tongue and the pharynx, hemorrhagic diathesis, skin lesions of the type of mycosis fungoides and formation of nodules or tumors in various organs, especially on the lymph nodes. The blood and bone marrow contain monocytes and monocytoid cells almost exclusively. The blood-forming organs produce cells of the monocytoid series only. This constitutes 95 per cent of blood cells formed in the sternal bone marrow. The spleen, all the organs, the lymph nodes and the newly formed nodules and tumors are the site of a massive invasion by monocytic cells. The existence of a pure form of monocytic leukemia is undeniable. The disease is due to a pathological disorder of the blood-forming organs, with production of tumor cells of the monocytic series only. These cells originate in either the undifferentiated mesenchymal cells or the reticuloendothelial system, with a possible transformation of pathological myeloblasts into monocytes. Monocytic leukemia is not a reticulosis, but is related to it, as are all other types of acute leukemia.

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BOOK REVIEWS

Williams Obstetrics. By Nicholson J. Eastman, Professor of Obstetrics, Johns Hopkins University, and Obstetrician-in-Chief to the Johns Hopkins Hospital, Baltimore. Tenth edition. Cloth. $12.50. Pp. 1176, with 659 illustrations. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, 1950.

Long used as a standard textbook in many medical colleges, this volume has been extensively rewritten. An attempt is made to orient the student to obstetrics in relation to society and medicine before consideration of the factual data of the text. Particularly gratifying is the standardization of definitions of various terms commonly used in obstetrics arrived at by agreement between the editors of the various textbooks. The standardized terminology is used throughout the text.

The chapter on toxemias of pregnancy is especially commendable for its clarity and excellence in classification. Since toxemias of pregnancy are now probably the leading cause of maternal mortality and our present methods of treatment are largely prophylactic and symptomatic, future reduction of maternal mortality must be made in this field by better understanding and development of more specific methods of treatment.

The new edition eliminates many of the references to the older works in obstetrics. This cutting away of the past is desirable for the medical student and the practitioner, who are chiefly interested in modern methods and technics. The illustrations, some of which are in color, are uniformly excellent. The volume as a whole represents a much needed and highly successful revision.

The Esophagus and Pharynx in Action: A Study of Structure in Relation to Function. By William Lerche, M.D. Cloth. $5.50. Pp. 222, with 93 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; The Ryerson Press, 299 Queen St., W., Toronto 2B, 1950.

According to the author, the primary purpose of the research described in this handsomely illustrated monograph was to throw light on the closing mechanism at the cardia. After the constrictor cardiae had been found in contraction in specimens that had remained in the state of regurgitation, Lerche's study was extended to an investigation of the relation of structure to function in the stretch of alimentary canal from cardia to pharynx during acts of regurgitation and deglutition. The various theories dealing with the closing mechanism at the cardia still suggest that a variety of problems pertaining to anatomy and physiology remain unsettled. Although it has limited appeal, this monograph should interest anatomists, pathologists and surgeons who are concerned with the relation of structure to normal and disturbed function of the esophagus and pharynx and with the action of the upper esophagus and pharynx.

Principles of Internal Medicine. T. R. Harrison, Editor-in-Chief. Editors: Paul B. Beeson, William H. Resnik, George W. Thorn and M. M. Wintrobe. Cloth. $12. Pp. 1590, with 245 illustrations. The Blakiston Company (Division of Doubleday & Company, Inc.), 1012 Walnut St., Philadelphia 5, 1950.

This book is intended primarily for the student and the general practitioner. In keeping with the modern trend in teaching, the authors attempted to integrate the preclinical sciences with clinical medicine so as to present the subject from the viewpoint of abnormal physiology, chemistry and psychology, as well as from the viewpoint of structural alterations. The emphasis throughout is placed on common disorders and basic principles rather than on rare clinical entities. The arrangement of the subject matter reflects the same general idea. The functional approach to the principles of internal medicine is covered in the first five parts of the book. The last two parts deal with specific infectious diseases and diseases of organ systems. Part 1, under the heading of Cardinal Manifestations of Disease, includes discussions of the major symptoms and signs of circulatory failure, renal failure and anemia. Part 2, Physiologic Considerations, deals with principles of particular interest in internal medicine. Part 3 discusses reactions to stress and to antigenic substances, fever and alterations in leukocytes. Part 4, Metabolic and Endocrine Disorders, also covers the nutritional disturbances. Parts 5 and 6 deal with disorders due to chemical and physical agents, and diseases due to biologic agents. There is a brief discussion of radiation injury and of the medical aspects of atomic explosions. Part 7 contains chapters dealing with the general management of infectious diseases and with the use of antibiotics. Each chapter contains brief, pertinent, biblographic references. The paper and print are excellent. This work will be a welcome contribution to the modern textbooks of internal medicine.

Allgemeine und spezielle Therapie der Geistes- und Nervenkrankheiten. Von Professor Dr. Friedrich Meggendorfer. Cloth. 22.50 marks. Pp. 235, with 49 illustrations. Wissenschaftliche Verlagsgesellschaft m.b.H., Tübinger Strasse 53, Stuttgart 1, 1950.

In his preface, the author of this book says he has tried to give a picture of present practices in the treatment of nervous and mental diseases for the use of newcomers in that field of specialization. He has avoided discussing the theoretical bases of the various treatments as well as the critical appraisal of results. This limits the usefulness of the book but enables the author to cover an extremely broad subject in interesting, readable style. It also affords an excuse for inclusion of some questionable therapeutic procedures, such as the application of short wave diathermy by means of air-spaced electrodes to the patient's head (page 56), the use of radon-water baths for arteriosclerosis and nervous disorders in old age (page 61) and the administration of hydroelectric baths (page 51). It remains to be seen whether American experience will confirm the European reports of excellent results from the treatment of neuralgia, especially sciatica, by means of ultrasonic vibrations; the author mentions three brands of generators for this purpose (page 57). The book is attractive in appearance and well indexed.

To Prospective Mothers. By William E. Hunter, M.D., F.A.C.S., and Bernard H. Smith, B.A., M.D., Attending Obstetrician and Gynecologist, Saint John's Hospital, Santa Monica, California. Cloth. $2.50. Pp. 161, with 12 illustrations. Bruce Humphries, Inc., 30 Winchester St., Boston 16, 1950.

This small handbook has been written with the currently-popular purpose of educating prospective mothers in the essentials of physiology and maternal care and, to some extent, pediatrics. In the final analysis, the utility of this effort must depend on a statistical study made among patients who read, a declining element in the American population. Certainly, practitioners will not approve unanimously any single work of this kind—some like a brief pamphlet containing essentials in lay terms, others, a more elaborate volume, and some few old-fashioned ones will persist in talking to their patients.

Most young women, especially those pregnant for the first time, enjoy "reading up" on the subject. Their ability to grasp this knowledge and apply it intelligently may be debated, but a book containing a number of vivid illustrations will enliven that deadly moment when the bridge scores are being compiled. Few will agree that "this cost [of good care] is the greatest single factor responsible for the low birthrate among the well-to-do." This statement not only is untrue, but reflects unfavorably on the profession and sounds an economic motive

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expressed more bluntly in the paragraph immediately following (and better omitted). Speaking of good care, the authors state, "Those mothers with comfortable incomes demand it," and, by inference, they say that the poor do not get this care. "Unless he [the obstetrician] submits, his patients switch to even higher-priced specialists" this is undignified, is fodder for the proponents of the welfare state and is poor advice for recent medical graduates. One can see little need for the preface to this book; the authors have tried too hard to break down the physician-patient relation in a day when this structure shows too well a crumbling foundation.

The mechanical features of the book, type, arrangement, pen and ink sketches and general readability, are good. There are a few misspelled words, and some technical statements are not generally accepted by the profession.

Cancer of the Colon and Rectum: Its Diagnosis and Treatment. By Fred W. Rankin, B.A., M.A., M.D., Surgeon, St. Joseph's Hospital, Lexington, Kentucky, and A. Stephens Graham, M.D., M.S., F.A.C.S., Surgeon, Stuart Circle Hospital, Richmond, Virginia. Second edition. Cloth. $7.50. Pp. 427, with 148 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; The Ryerson Press, 299 Queen St., W., Toronto 2B, 1950.

This edition of this excellent book represents the further work of the authors, along with that of many American and British surgeons. It attains its goal, "to create constructive thought and criticisms which will further forward the efforts toward both cure and palliation of a lamentable malady." It brings up to date all the work that has been done in the specialty of Dr. Rankin and his associates. The book is profusely illustrated throughout with detailed drawings of anatomy, pathology and surgical technic. It contains statistical results of many workers regarding the incidence and occurrence of colonic and rectal carcinoma and their morbidity and mortality.

While this edition, like the first, is intended largely for surgeons, explaining in some detail operative technic, it should be realized that it is a worth while book for internists, especially those interested in gastroenterology. To the latter group it gives some insight in the choice of operation, as well as the preoperative and postoperative management. The authors prefer a one stage abdominal perineal or perineal abdominal resection wherever possible; if the carcinoma is below the peritoneal reflection, they recommend colostomy and perineal excision.

The book is readable; the subject index and author index are ample, and the bibliography at the end of each chapter is complete and up to date. This book should be in the library of every surgeon, especially those specializing in abdominal surgery. It is also a good reference for students. Finally, internists and gastroenterologists will be able to utilize the factual information, which is presented in a logical manner.

An Atlas of Human Anatomy. By Barry J. Anson, Ph.D., Professor of Anatomy, Northwestern University Medical School, Chicago. Cloth. $11.50. Pp. 518, with illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1950.

This atlas is divided into the following sections: head, neck, upper extremity, back and thorax, abdomen, pelvis and perineum and lower extremity. The drawings accurately depict anatomy as seen in the cadaver. The illustrations dealing with the skull are well presented. However, the adult male skull viewed from below, as seen on page 5, seems to be somewhat out of proportion.

The author has attempted to show magnification in various locations by a drawing of a magnifying lens on the illustration. This is effective as presented on page 55, where a large hand lens magnifies a section of the parietal bone; unfortunately, however, the effect might be overlooked on page 15, figure B, where the magnifying lens is presented in a diminutive form. The use of the insert, as in figure B on page 34, adds much to the understanding of the three divisions of the trigeminal nerve. On page 37 the result of careful research work pertaining to the facial nerve is presented. The illustration is excellent wherein the major types of facial nerve branchings and their anastomoses are presented in conjunction with the percentages of occurrence of each type. The presentation of the subject of the triangles of the neck is cleverly depicted on page 69. With the use of inserts, the various triangles have been inked in and thereby show the extent of the boundaries of each individual triangle. Such presentations have distinct teaching value. No mention was made of the cricopharyngeus muscle. If the author believes that no such special muscle bundle exists, that statement would have helped to clarify the question of whether such a "pinchcock" muscle is present. On page 93 one notices that the inferior constrictor muscle of the pharynx merges directly into the esophageal musculature. One wonders why the use of the conventional red for arteries was not adhered to. In many of the illustrations the arteries are presented in black. This might cause some confusion where two different colors are used for similar structures on opposing pages, as, for example, on pages 220 and 221. The abdominal aorta is presented in red on page 220 and the bronchial arteries in black on page 221.

Particularly well presented are the variations in the extent of the fleshy portions of the internal oblique and transverse abdominal muscles as seen on page 257. The percentage figures of these variations are superimposed on the drawing. Such studies are helpful to the surgeon. The section pertaining to the female perineum and female pelvis is especially well done, particularly the color plates on pages 378 to 384 inclusive, which beautifully present the blood supply to these regions. Although the subject matter on page 494 regarding femoral hernia is well presented, orientation nevertheless is difficult. An intact inguinal ligament as a landmark would have helped these figures tremendously.

This volume represents the culmination of many years of thorough investigative work. It is written in authoritative fashion by an authority. The Atlas might have been more appealing to the average student and surgeon if more anglicized terminology had been used. The book can truly be called an anatomist's anatomy and can be recommended as a reference volume for anyone interested in the subject.

Geriatric Nursing. By Kathleen Newton, R.N., M.A., In Charge of Graduate Nurse Education, Cornell University-New York Hospital School of Nursing, New York City. Cloth. $4.50. Pp. 420, with 42 illustrations. The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1950.

In view of the rapidly increasing interest in geriatrics, this volume in geriatric nursing is timely and altogether commendable. In excellent fashion it meets the needs of the nurse who desires to take care of the aged both at home and in the hospital. The book reflects an extensive experience and rare good judgment on the part of the author. She discusses in an enlightening and interesting manner the problems and technics concerned in caring for elderly people. The discussion covers not only the physical ills of the patient but also their social and psychological needs. The subject matter is well organized and indexed to good advantage. The references in each chapter are numerous and well chosen. The illustrations are plentiful and attractive, as well as being instructive. From the publisher's standpoint the book leaves little to be desired.

Adrenal Cortex: Transactions of the First Conference, November 21-22, 1949. Edited by Elaine P. Ralli. Associate Editors: Konrad Bloch and Gregory Pincus. Cloth. $2. Pp. 189, with illustrations. Josiah Macy, Jr., Foundation, 565 Park Ave., New York 21, 1950.

A particularly interesting discussion in this volume is the one on steroid metabolism, in which it was indicated that continued administration of pituitary adrenocorticotropic hormone (ACTH) in normal human subjects results in a precipitous fall of total cholesterol values, chiefly of the ester fraction. This fall generally occurs between the third and fifth days. Prior work has shown that there occurs a sharp fall in the adrenal cholesterol content when animals are subjected to stress or when epinephrine or pituitary adrenocorticotropic hormone is administered. The present observation is suggestive, since it apparently indicates the source of the cholesterol presumably used in the synthesis of adrenal steroids. This is a valuable monograph for those who desire fundamental knowledge concerning the adrenal cortex.

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QUERIES AND MINOR NOTES

ALCOHOL AND FERTILITY

TO THE EDITOR:—*A well developed adult white man, 27 years of age, married two years, has asked my opinion on his procreative ability. A fresh, carefully transported specimen of semen was examined by an accredited laboratory, with the following report: volume, 8.5 cc.; motility, 50 per cent; juvenile or immature forms, 25 per cent; headless tails, 25 per cent, and actual count, 34,600,000 per cubic centimeter, as compared with a normal count of 70 million or more. What is the probability of impregnation by this man? How soon are the spermatozoa affected after the ingestion of considerable amounts of alcohol, and how does it affect them?*

Robert Taylor, M.D., East Haven, Conn.

ANSWER.—To some extent the unusually large volume of the ejaculate in this case might compensate for the relatively low count per cubic centimeter. As to the subnormal motility, one would like to be sure that the specimen was not collected in a rubber condom, for many of these articles contain chemicals that are rapidly lethal to spermatozoa. The morphology is poor, and the over-all picture suggests a moderately severe grade of infertility. Final conclusions should be withheld until several other specimens have been examined. If the findings here reported are found to be constant, the chances are against this man's being able to impregnate a woman of average fertility, though the possibility is always present.

As far as known, the ingestion of large amounts of alcohol on any single occasion has no immediate effect on spermatogenesis. Chronic alcoholism, on the other hand, may operate, as do many other types of chronic intoxication, to depress or even to inhibit the functioning of the seminiferous tubules.

SPERMATOZOA AND VAGINAL ACIDITY

TO THE EDITOR:—*Is it rare for pregnancy to result from deposition of sperm on the vulva without intromission? How rapidly does the normal vaginal acidity kill spermatozoa, if at all?*

M.D., Rhode Island.

ANSWER.—It is rare for pregnancy to follow deposition of the sperm on the vulva without intromission. Sperm may remain alive in the vagina for a number of hours. When Huhner tests are done, some living sperm may be found seven and eight hours after coitus. Normally, however, only about 10 per cent of the spermatozoa are alive in the vagina two hours after coitus (Siegler, S. L.: Fertility in Women, Philadelphia, J. B. Lippincott Company, 1944). Vaginal acidity by itself does not cause sterility.

DESENSITIZATION TO HORSE DANDER

TO THE EDITOR:—*A 35 year old man is allergic to horse hair. His eyes swell shut and he has a profuse nasal discharge within 30 minutes after contact with horses. He is a specialist in a field of animal husbandry that requires frequent contact with horses. What is available for treatment other than the antihistaminic drugs?*

Preston L. Hathcock, M.D., Fayetteville, Ark.

ANSWER.—Desensitization to horse dander is possible, although the degree of protection required in the type of exposure described is not always possible of achievement. In a situation where a professional career is at stake it is certainly worth trying. A potent extract of horse dander should be procured. The initial dose, to be given subcutaneously, will depend on the degree of sensitivity as shown by skin test and would probably be about 0.05 cc. of a 1:100,000 or 1:1,000,000 dilution. Increments of about 25 per cent of preceding doses are usual. When a dose of 1 cc. of the dilution is reached, the next stronger concentration is begun. The first several doses can usually be given frequently, two to three times a week or even every day. A semiweekly schedule is then established and usually maintained until maximum doses are achieved or until the patient shows evidence of good clinical protection. The maximum concentration used in desensitization is usually 1:100. After protection is established maintenance doses are usually required. Depending on the individual circumstances these may be indicated at intervals of one to four weeks.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

MOLD IN HOME FURNISHINGS

TO THE EDITOR:—*Rhinitis and asthma developed in a 45 year old woman two years ago, while she was living in Warsaw, Poland. This ceased on her return to this country but returned one year later, when she moved into a house containing some of the rugs and pads of the former occupant. Intradermal tests showed sensitivity to Hormodendrum, and cultures from the house revealed the fungus to be present in large numbers. Is there some procedure by which one can effectively rid this house of the mold?*

William G. Woodin, M.D., Syracuse, N. Y.

ANSWER.—Hormodendrum is the commonest air-borne spore that will grow on laboratory mediums. Before it is concluded that the house is the source of this organism, a direct simultaneous comparison should be made of the number of colonies obtained from the outdoor air. For example, on many days in the summer a petri plate exposed outdoors for 15 minutes will show in a few days about 10 to 30 colonies. If the plate is exposed for 24 hours it will be overgrown with Hormodendrum. Airing, drying and sunning will destroy most of the mold that may be present in the home furnishing. The pads and rugs may be aired outdoors, preferably in direct sunlight. Damp places, such as the basement, may be dried by drying agents, such as calcium chloride. Commercially available fungicidal sprays that are used to inhibit molds on plants might be used. Ultraviolet rays have also been used for this purpose.

ALKALINE PHOSPHATASE IN OBSTRUCTIVE JAUNDICE

TO THE EDITOR:—*Why is the serum alkaline phosphatase level raised in most cases of obstructive jaundice, and why is the cholesterol esters level lowered then?*

J. Schouten, M.D., Rotterdam, Holland.

ANSWER.—Large amounts of alkaline phosphatase are excreted in the bile. The increase in alkaline phosphatase in the blood stream in cases of obstructive jaundice is presumably due to the fact that the normal means of excretion has been blocked. Other hepatic causes for increase in serum alkaline phosphatase are hepatocellular jaundice and metastatic carcinoma to the liver. In such instances the increases are probably due to intrahepatic obstruction and are usually of a lesser degree as compared with obstruction of major bile ducts.

There is some evidence that the simple explanation of retention of alkaline phosphatase is not the whole answer to the question. It has been reported that no rise occurs in infants with congenital atresia of the bile ducts. It has also been reported that there is a pronounced rise in external biliary fistulas, which falls to normal when the fistulas are repaired. It must also be remembered that there are other extrahepatic causes for alteration in the serum alkaline phos-

phatase, such as Paget's disease of bone, parathyroid adenomas and metastatic carcinoma to bone.

The cholesterol esters are usually increased in obstructive jaundice. This increase usually parallels the increase in non-esterified cholesterol, so that the ratio between the two remains normal. When the cholesterol esters are found lower than normal in relation to an elevated cholesterol level (normally the cholesterol esters are 60 to 80 per cent of the total), it is probable that there is superimposed hepatocellular damage. Consequently a lowered cholesterol ester ratio in the presence of obstructive jaundice may be of serious prognostic significance.

LARGE BREASTS IN YOUNG WOMAN

To the Editor:—*Is there any treatment for reducing the size of the female breast? The patient is a girl of 20; her breasts have been gradually increasing in size until now they are of such proportions that they embarrass her. Her basal metabolic rate is —12 per cent; she has been receiving thyroid for several years. There appear to be no other abnormalities.*

M.D., New York.

Answer.—The size of the breasts should be disregarded unless they become unusually engorged, red and very tender preceding menstruation. If they become definitely red and tender, small doses of methyltestosterone (10 mg. daily) may be helpful. Large doses should not be used, because of the danger of masculinization. No treatment should be given if the breasts merely appear to be large and show no sign of abnormality.

PHLEBOTOMY IN HYPERTENSION

To the Editor:—*Is there any indication for phlebotomy in hypertension? A patient has a blood pressure of 220/120, but there is no decompensation. What is the best way to perform a phlebotomy in the office or in the home of the patient? How much blood should be removed?*

M.D., New York.

Answer.—There is no indication for phlebotomy in hypertensive disease in the absence of cardiac decompensation, except in those rare and exceptional instances in which the hypertension is secondary to polycythemia vera. For a more complete explanation the inquiring physician is referred to the reply to an almost identical question in Queries and Minor Notes published in The Journal April 19, 1947.

CHOLESTEROL

To the Editor:—*I have heard the suggestion that cholesterol is a faulty end-product of fat metabolism, bearing a position analogous to that of uric acid in protein metabolism. Has any work been done along this line?*

Bernhard A. Fedde, M.D., Brooklyn.

Answer.—Cholesterol is a product of metabolism but not necessarily of fat metabolism and not necessarily a "faulty product." Cholesterol is synthesized by the body from simpler substances which can be derived from fat, protein or carbohydrate. Cholesterol so formed is referred to as endogenous cholesterol. Exogenous cholesterol is that received as such from dietary sources. Much research on cholesterol metabolism is in progress.

MORTALITY IN INTERVERTEBRAL DISK OPERATIONS

To the Editor:—*What is the mortality in intervertebral disk operations?* *Walter L. O'Nan, M.D., Henderson, Ky.*

Answer.—The mortality in operations on the lumbar intervertebral disks is extremely small. In a series of 500 consecutive cases there was one death (mortality rate of 0.2 per cent). This death occurred from postoperative pneumonia before the newer antibiotics were available. It is probable that the mortality rate following surgery on cervical intervertebral disks is slightly higher.

SHIGELLOSIS

To the Editor:—*What is the best treatment for intestinal infection in a case in which results of laboratory tests are positive for Shigella? Shigella organisms were discovered in a child at the age of 1 month, and death occurred at the age of 6 months. She was treated with sulfasuxidine, which resulted in normal stools. At the age of 5½ months her skeletal and muscular development was normal. Mild fever and vomiting, without diarrhea, then occurred. The stool was again highly positive for Shigella organisms. She was treated with sulfadiazine. Two days after treatment was started severe diarrhea suddenly developed. In spite of parenteral treatment with fluids, nikethamide and oxygen, she died within 12 hours.*

Levi Oberndorfer, M.D., Colombia, South America.

Answer.—Among the medicaments included in the treatment of Shigellosis in its active stage should be sulfathalidine in adequate amounts and sulfadiazine. In the severe cases the two may be used in combination. Aureomycin has proved to be a useful antibiotic in many of these cases. The importance of supportive measures, including fluid balance and attention to the various minerals and metabolites, is of greatest importance.

MEIBOMIANITIS

To the Editor:—*A patient who was treated surgically for cataract is getting along well but has a white, frothy discharge or accumulation in the conjunctival sac. The only condition I can find in the literature resembling it is meibomianitis. However, expression of the glands yielded nothing; zinc and antibiotics have not been of help. Culture showed nothing. I would like some help in diagnosis and treatment.*

M.D., New Mexico.

Answer.—The frothy discharge certainly seems to be the mixture of oily material, air and tears which comes with meibomianitis. Zinc and other drugs have been of little avail in similar cases. The use of hot applications may be of some help.

USE OF ULTRAVIOLET AND INFRA-RED RAYS

To the Editor:—*I wish to know whether ultraviolet and infra-red rays in office practice may be used on the skin of colored patients. Is there any difference between its use in the colored patient as compared with the white patient?*

M.D., New York.

Answer.—The use of ultraviolet and infra-red rays in office practice may be used in any indicated skin condition regardless of the patient's race. One must remember that blondes, as a rule, are more sensitive to light rays than brunettes and light-skinned colored patients are generally more sensitive to ultraviolet rays than dark-skinned ones.

CRYOTHERAPY

To the Editor:—*What are the temperatures of liquid oxygen, solid carbon dioxide and liquid nitrogen as used in cryotherapy?* *Everett C. Ravits, M.D., Hackensack, N. J.*

Answer.—The requested temperatures are as follows: liquid oxygen, 110 F.; liquid nitrogen, 321 F., and solid carbon dioxide, 110 F. The temperature of solid carbon dioxide is lowered considerably on the addition of acetone.

TREATMENT OF RABIES

To the Editor:—*What is the best treatment for acute rabies?*

J. M. Covington Sr., M.D., Wadesboro, N. C.

Answer.—Rabies is a fatal disease. There is no cure. Therefore, treatment must be symptomatic. Restraints should always be applied, whether or not the patient is having convulsions. Morphine may be required to control excitability, but in late stages there may be deep stupor.

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